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Rhabdomyomatous Dysplasia of the Lung

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Summary. Case report of a 4 months old child with systemic involvement of cross-striated muscle tissue of different grade of maturity in alveolar septa and bronchial walls of a hypoplastic lung. After a morphological description, a short review of the literature is followed by the discussion of formal pathogenesis of this rare pulmonary malformation.

Case Report

After a normal pregnancy and delivery, the neonate of a 23 years old primipara showed symptoms of Respiratory-Distress-Syndrome. Chest-X-rays revealed dextrocardia, a hypoplastic left lung and highly decreased respiratory excursions. Chromosomal-Analysis was normal (46 xx). Although artificial mechanical respiration was performed, increasing respiratory failure occurred, and the child died 4 months after birth.

The autopsy revealed multiple mainly cardiovascular and pulmonary malformations: The left pulmonary artery was highly hypoplastic with a narrowed lumen, the right pulmonary artery was slightly dilated; there was an infantile coarctation of the aorta, a widely open ductus arteriosus Botalli and a patent foramen ovale. The left lung filled only the upper part of the left thorax, it was hypoplastic and showed no lobation. The caudal parenchyma was dark-reddish and firm, it displayed a diffuse basal accretion with the diaphragm which was dislocated cranially into the left thorax. No diaphragmatic hiatus or hernia could be detected.

Histological Findings

The basal parts of the lung are not well differentiated. There are no mature alveoli, the air spaces consist of terminal bronchioli. The number of small bronchi in relation to square-units is increased. The terminal respiratory bronchioli rarely show alveolar formation and contain many desquamated alveolar or respiratory epithelial cells (Fig. 1). The septa and bronchiolar walls are thickened and contain bundles of muscle fibers with a well recognizable cross-striation (Fig. 2). They circumfere rete-like the respiratory air spaces and are also found in the walls of larger bronchi, there intermingled with smooth muscle cells. The striated muscle-fibers measure up to 200 μm in length and 15 μm in thickness, they show a bright eosinophil cytoplasm and big nuclei, sometimes forming multinucleated giant cells, and they lie between capillaries and respiratory epithelium (Fig 3). The polarized light and PTAH-stain reveal typical cross-striation of sceletal muscle-fibers.

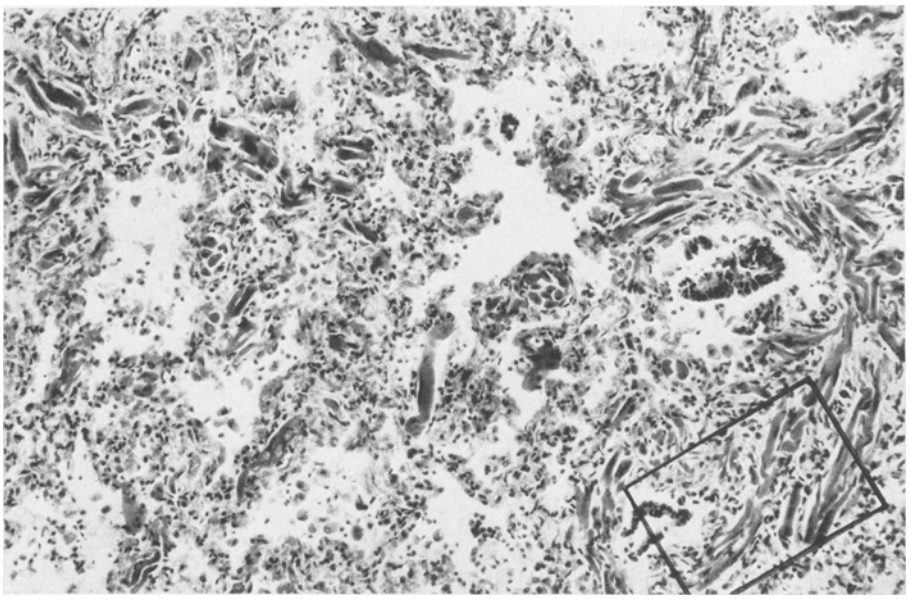

Fig. 1. Pulmonary rhabdomyomatous dysplasia: Immature lung-tissue with desquamated alveolar and ciliated respiratory epithelial cells in terminal bronchioli and differentiating alveoli. Septa are enlarged and show longitudinally and cross-sectioned sceletal muscle-fibers. (Formol-Paraffin, HE, ×120)

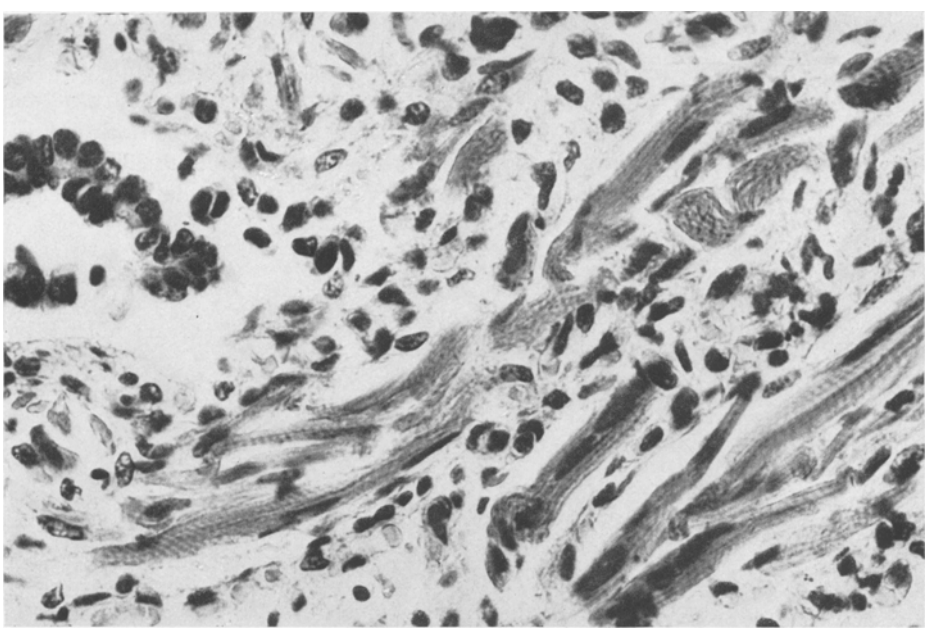

Fig. 2. High power view of inset in Fig. 1 showing large cross-striated muscle bundles curling around bronchiolar spaces. Note different maturity of muscle tubes with central or marginal location of nuclei. (Formol-Paraffin, HE, polarised light, ×480)

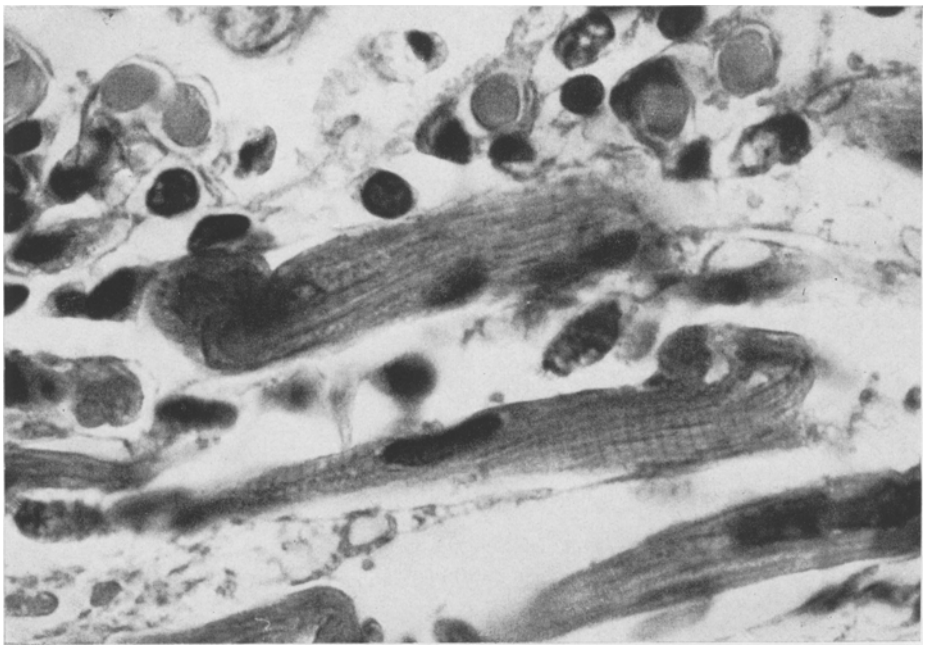

Fig. 3. High power view of bronchiolar septum showing cross-striation of interlacing sceletal muscle fibers between capillaries and respiratory epithelium. (Formol-Paraffin, HE, polarised light, ×1200)

Electron Microscopy

Material from paraffine blocks of lung tissue was deparaffined and reembedded in Epon (for details see Hübner, 1970); semithin and ultrathin sections were prepared and processed as usual for light and electron microscopy.

As already observed in semithin sections, the sceletal muscle cell elements contain one or multiple nuclei, which are either arranged in the middle of the cell or on its periphery. The chromatin mostly is distributed marginally, the nucleolus is prominent. Well differentiated myofibrillar bundles occupy the cytoplasm. In some of the cellular elements the myofibrils are oriented in different directions, so that longitudinally and transversely sectioned myofibrils lie side by side (Fig. 4). In the longitudinally sectioned myofibrillar bundles, especially in those sceletal muscle fibers, where the fibers are all longitudinally oriented, A- and I-bands as well as typical Z-lines can be distinguished. The medium distance of the Z-lines is about 3 μm, the A-band measures approximately 1.5 μm. Clusters of ribosomes are arranged between the myofibrillar bundles (Fig. 5). Remnants of swollen mitochondria often are arranged between longitudinally sectioned muscle fibrillar bundles. Because of the unappropriate preparation and the autolysis of the specimen further fine structural details cannot be evaluated.

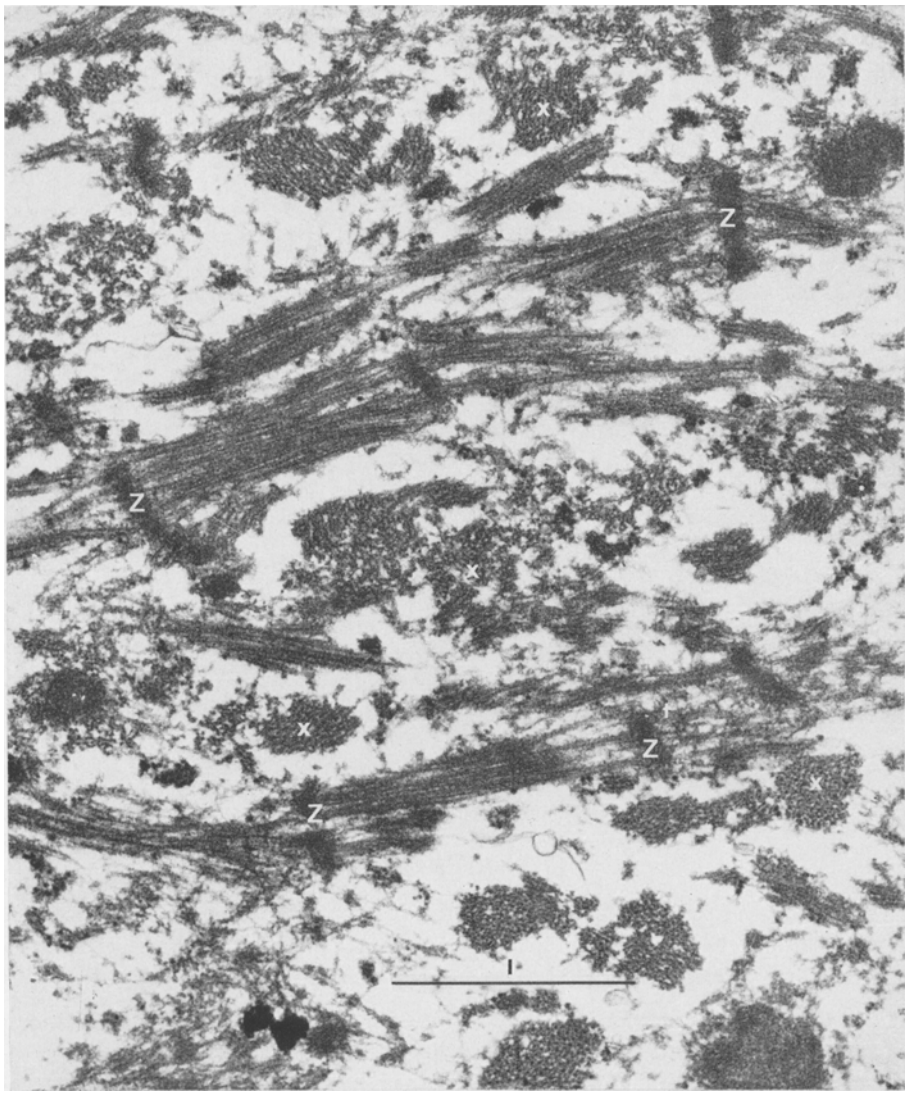

Fig. 4. Electron micrograph shows part of sceletal muscle fiber containing bundles of myofilaments cut either longitudinally, transversely (x) or obliquely. Z = Z-line. (Formalin-fixed autopsy material, ×41000, Arch. Nr. 4225)

Discussion

There are only few reports found in the literature to similar lung-changes:

Zipkin in 1906 published the case of a 33 week-foetus:

The left lung was increased in size, reddish-gray and firm, it showed small cysts on the base and bronchi and vessels on the cut surface. Microscopically the abundant vascular stroma as well as the muscular coats of the bronchi contained many cross-striated muscle-fibers. The histological findings are documented

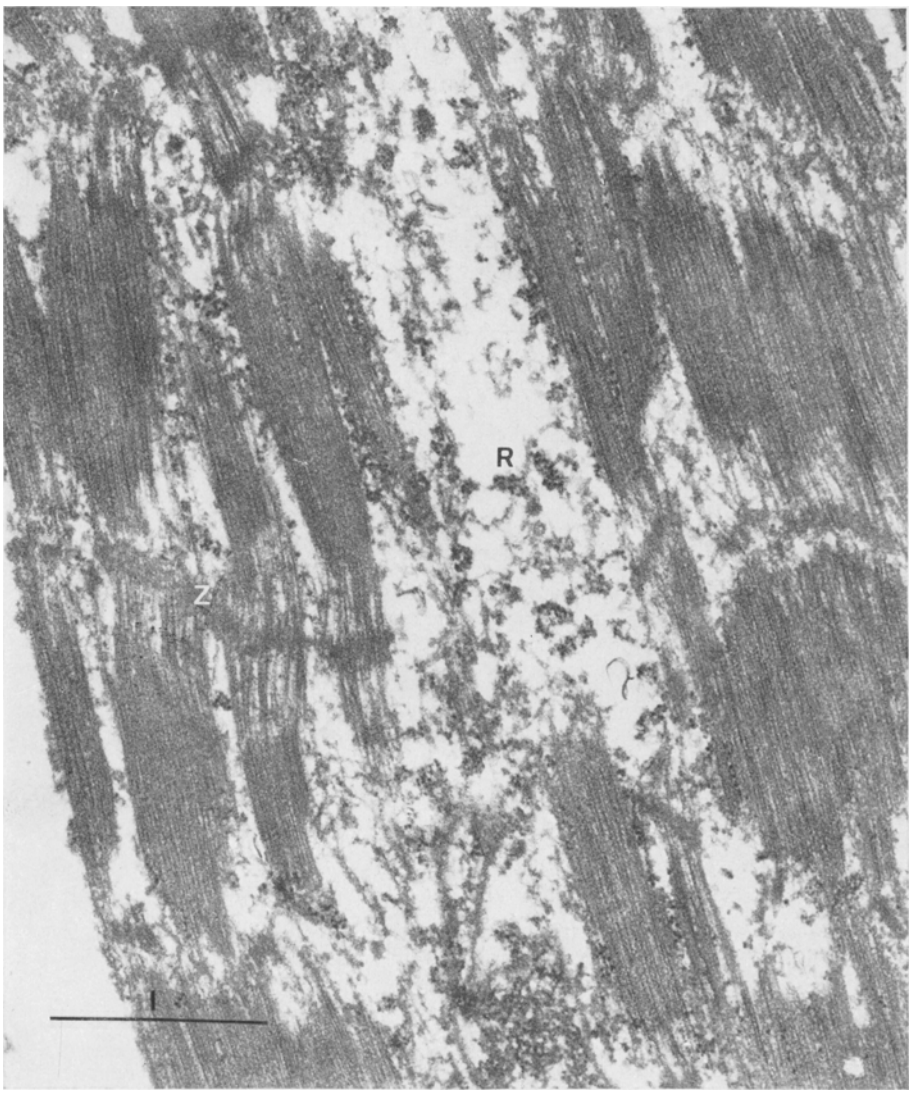

Fig. 5. Electron micrograph shows part of sceletal muscle fiber with parallel bundles of myofibrils divided in distinct I-bands and less distinct I-bands. In the middle of the I-band the Z-line (*Z*). Between the bundles of myofilaments many ribosomes (*R*). (Formalin-fixed autopsy material, ×32000, Arch. Nr. 4221)

by excellent drawings and are similar to the described alterations in our case. The only difference is a sharp limitation against the normal lung tissue by fibrous connective tissue and the occurrence of cross-striated muscle-fibers in the pleura, we could not observe in our case. Because of the striking increase of adenoid structures, obviously consisting of immature or dysplastic bronchi, limited by a cuboidal ciliated epithelium, Zipkin called this pulmonary alteration adeno-rhabdomyoma.

The pathogenesis of this adenorhabdomyoma was regarded as combination of adenomatous proliferation of epithelial lung-primordium and dislocated embryonal muscle-fibers provening from adjoining myotomes, that means a "teratoid arising in an already differentiated lung tissue".

Potter (1953) described a closely similar case of a 780 g stillborn foetus:

The lungs appeared slightly enlarged, the number of blood vessels was increased, the bronchi were normal. The distal parts of the pulmonary tree were hypoplastic and no normal alveoli could be found. "In regions, where the blood-vessels were largest and most numerous there were large interlacing masses of striated muscle cells". The increase of blood vessels induced Potter to call this malformation a "haemangiorhabdomyoma".

Willis (1962) mentions histological findings in a 5 week old South-Australian infant, showing "plentiful cross-striated muscle-fibers in the lung", but there are no closer details or description concerning this case.

Lung neoplasms containing cross-striated muscle-fibers and primary pulmonary rhabdomyosarcomas are rarely described (Spencer, 1968; Eck, Haupt and Rothe, 1969; Liebow, 1952; Müller, 1928; Otto, 1970; Fischer, 1931). In this group of lesions obviously also belongs the much cited case of Helbing (1898):

The left lung of a 23 years old man was replaced by a white lobular mass with chondroid nodules, cysts and large bundles of connective tissue. There were no blood vessels nor bronchiolar lumina. The histological examination revealed epithelial cysts and adenoid formations as well as undifferentiated mesenchymal cells, hyaline chondromatous tissue and cross-striated muscle cells with giant cell formation.

This description of the microscopic changes gives the impression of a malignant teratoma.

In contrary to the opinion of Spencer (1968) we do not include the case of Zipkin (1906) into the group of primary pulmonary blastomas. This case as well as the pulmonary lesion described by Potter (1953), which is also identical with our own observation, is not a real blastoma with autonomous, expansive or infiltrating growth, nor are there any criterias for malignancy.

Light and electron microscopy show, that the sceletal muscle cell elements in the lung display different grades of maturity. Immature elements have centrally oriented nuclei and often myofibrillar bundles oriented in variable directions. They might be marked as myotubes. Other elements show higher degrees of maturity with marginally located nuclei, distinct A- and I-bands with typical Z-lines.

The systemic integration of striated muscle-fibers in the alveolar septa and bronchiolar walls of a dysplastic and immature pulmonary parenchyma rather reveals a systemic error in the general plan of development. It could be named a generalized pulmonary hamartoma, if the term "hamartoma" would not have been restricted to "inborn errors of tissue development of normal constituents of an organ, characterized by abnormal mixture of tissues indigenous to the part with excess of one or more of these" (Albrecht, 1904; Willis, 1962). As sceletal muscle-fibers are not normal constituents of the lung, we conclude that it rather points to a systemic integration of heterotopic muscle tissue in a differentiating immature lung.

In contrast to Willis (1962), who suggested that sceletal muscle-fibers might have developed by heteroplasia from undifferentiated mesoblastic cells in the

lung itself, we believe them to be misplaced by extension from adjacent muscle tissue during development of the lung bud. Either they develop from heterotopic muscle tissue of the branchial or the pharyngeal pouch, or they arise from secondary ingrowth of diaphragmatic muscle germs into the lung primordium.

As parts of the muscular diaphragmatic primordium originate from myotomes of the 4th and 5th cervical segment and grow only secondarily into the mesenchymal septum transversum (Gruber, 1927), the fusion of developing lung primordium with heterotopic diaphragmatic muscle germs could also be possible.

The latter hypothesis would be supported by the additional diaphragmatic malformation with accretion of distal parts of the lung with the diaphragm. Further support gives the decreasing number of striated muscle-fibers from the base to the apex of the lung, restricting the heterotopic sceletal muscle-fibers to the caudal areas of the lung.

However, the systemic integration of heterotopic muscle cells into the texture of an already differentiated lung primordium remains extraordinary.

Until the origin of the striated muscle-fibers is definitely ascertained, in our opinion the most accurate nomenclature of this malformation would be "Pulmonary Rhabdomyomatous Dysplasia", or "Dysplastic Rhabdomyosis".

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