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Central Nervous System Heterotopia in the Lung of a Fetus with Cranial Malformation

E. Campo and J.A. Bombi

Cátedra de Anatomía Patológica, Facultad de Medicina, Universidad de Barcelona, Barcelona, España

Summary. Heterotopic glial tissue was seen within the lungs of a newborn with a cranial malformation and anterior spina bifida.

Histological examination of the lung showed solid islands of glial tissue intermingled with pulmonary structures. Well developed bronchioles that were in continuity with the main bronchial tree could be identified within the nodules. The central cystic cavity of the nodules is a bronchial lumen probably dilated by the respiratory movements. Several hypotheses have been elaborated to explain the heterotopic glial tissue in lung.

The presence of an anterior spina bifida suggests a migratory mechanism to explain the embryogenesis of this case.

Key words: Glial Heterotopia – Anencephaly – Heterotopia – Lung – Spina bifida.

Introduction

Central nervous system heterotopia in the lung is a rare abnormality. There are only a few reported observations in the literature and a precise embryogenetic hypothesis is lacking. Most reported cases are associated with major CNS malformations including anencephaly (Gruenwald 1941; Potter et al. 1942; Moragas et al. 1974; Kanbour et al. 1979), frontal meningocele (Hückel 1929) and microencephaly with encephalocele (Askanazy 1908). There is only one case in an adult with a normally developed skull and CNS, who died after a cerebrovascular accident (King 1938). Recently, a case with respiratory distress in a newborn with minimal malformation (micrognathia and fusion of the tongue to the floor of the month) has been reported (Gonzalez-Crussi 1980). The growth of glial tissue in the lung reflects the proliferative potential of the these cells in unusual environments, which is also seen in glial tissue within the peritoneal implants of some ovarian teratomas (Robboy et al. 1970; Nogales et al. 1976).

Offprint requests to: Dr. J.A. Bombi, Cátedra de Anatomía Patológica, Facultad de Medicina, Universidad de Barcelona, Casanova, 143; Barcelona 36, España

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The purpose of this paper is to add a new observation of this peculiar abnormality. An interesting relationship between the nervous tissue and the pulmonary bronchioles is observed. Moreover, we believe this is the first report of the association between CNS heterotopia in the lung and anterior spina bifida. This finding supports one of the pathogenetic hypotheses previously suggested (Kanbour et al. 1979).

Case Report

The patient, a white female infant, was born after 36 weeks gestation from a 28-years old mother, para 1 grava 1. Her first child is now 4 years old and was born by vaginal delivery after an uneventful pregnancy.

The second pregnancy was complicated by hydramnios and a cranial malformation was diagnosed by ultrasonography in the 36-th week. Delivery and placental expulsion were spontaneous. At birth, the weight was 1,600 g and crown to heel lenght was 40 cm. The infant was in poor condition with Apgar ratings of 4, 3, 2 at 1,5 and 10 min respectively and she died 12 min after birth.

At autopsy, the body showed and externally normal configuration of neck, trunk and extremities. Marked asymetry was evident in the facial structures. The right hand side of the face showed well developed hemi-mouth, tongue, facial bones and heminose, a rudimentary auricle and a eyeball located inside a small orbit. The left hand side of her face was markedly abnormal, showing very rudimentary eyeball, nose, auricle and a proboscis, similar to that of cyclopia. These structures did not maintain the usual topographical relationship. The left hand side of the hemi-mouth was lacking. The cranial vault was lacking and was partially replaced by the scalp and a big meningovascular bursa with haematic contents. Only part of the occipital bone, including the foramen magnum and some structures of the base of the skull could be identified in the cephalic skeleton.

Roentgenographic examination showed markedly abnormal cranial and facial skeleton. All the bones of the extremities were well developed. An anterior spina bifida was observed at the level of D VII.

Results

Gross examination of the organs revealed marked hypoplasia of both adrenals (0,57 g. both, expected 5 ± 2.0 g), mild renal hypoplasia (7.27 g both, expected 16 ± 4.0 g) an endothoracic thyroid gland and persistent urachus.

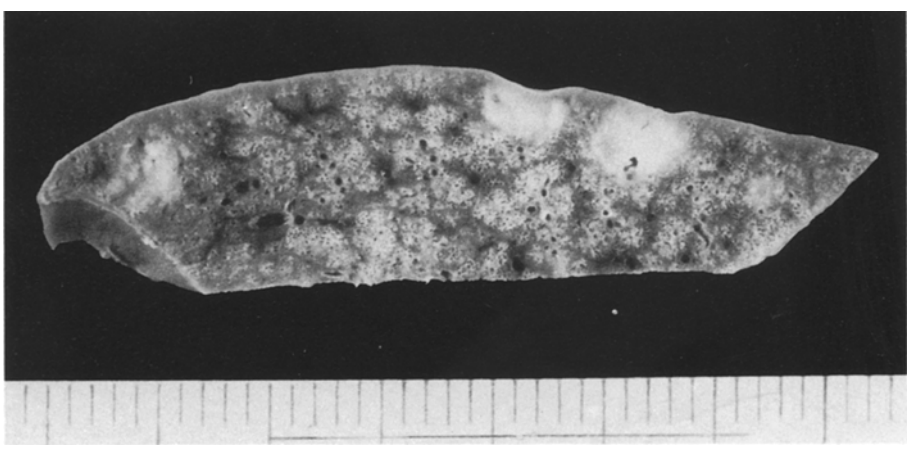

Fig. 1. A section of the left lung showed three nodules

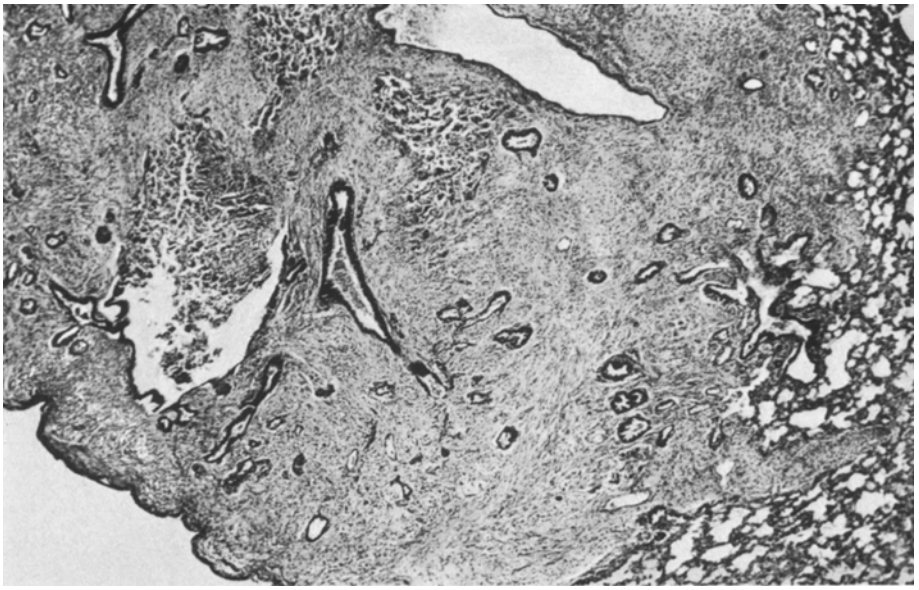

Fig. 2. The nodules of glial tissue showing well developed bronchioles inside them. 40 ×

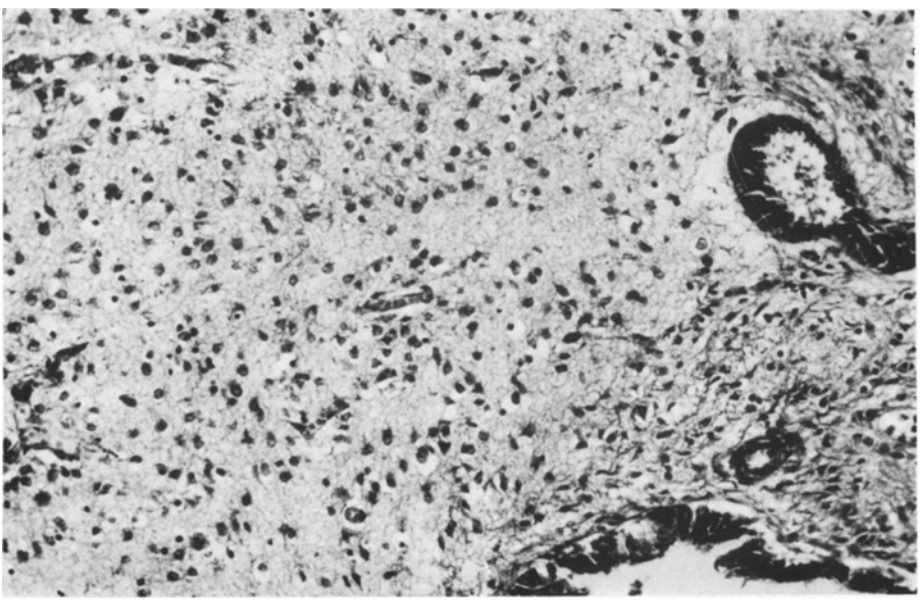

Fig. 3. The detailed structure of the glial tissue in the lung. 250 ×

The right lung weighed 17.57 g and the left one 14.42 g. They were remarkable in that multiple, well delimited, round, non-prominent nodules could be observed on the pleural surface, measuring from 0.2 to 0.6 cm in diameter. These nodules were diffuse and irregularly distributed over both lungs and involved all lobules. In sections, their subpleural location was evident (Fig. 1). A thin rim of lung

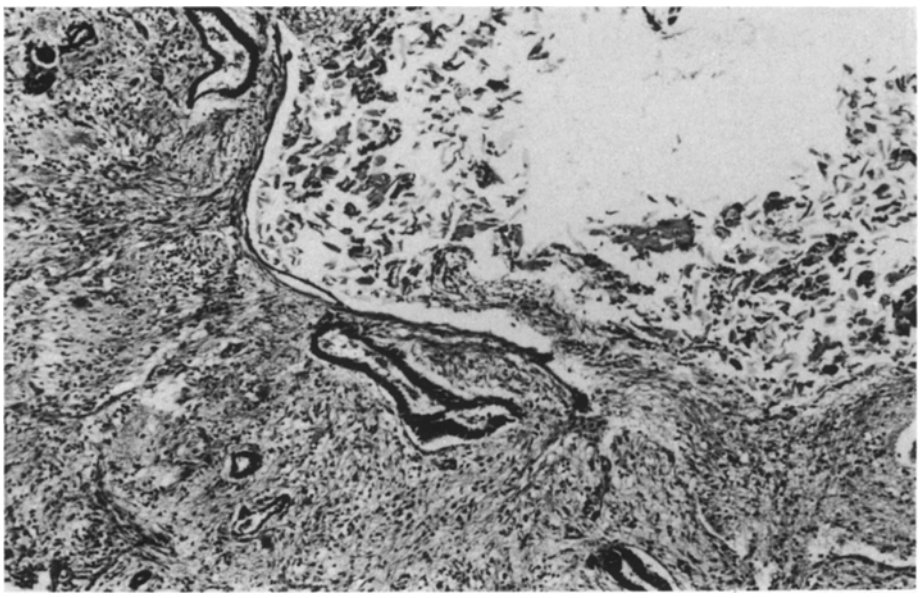

Fig. 4. Some of the nodules contain desquamated amniotic cells in one central cavity partially lined by epithelial cells. 100 ×

parenchyma was present between the pleura and some of them. A small cavity with cystic appearance could also be seen inside some of them.

The histological appearance of both lungs was similar. Well distended areas could be seen alternating with collapsed ones. Thick conective tissue walls were prominent at the periphery in contact with the pleura, indicating residual primitive lobulation. The nodules identified macroscopically corresponded to masses of glial cells and nervous fibres. The margins seemed to dissect the interalveolar space in some fields, while in others, they showed and expansile growth. Well developed bronchioles lined by ciliated cylindrical epithelial cells could be identified inside the nodules (Figs. 2 and 3). Continuity between bronchioles from inside the nodules and those from the lung parenchyma could ocasionally be observed. Some of these glial masses had a central cavity containing large eosinophilic epithelial cells with small hypercromatic nuclei, corresponding to aspirated and desquamated amniotic cells (Fig. 4). In one of the nodules, the cavity was partially lined by ciliated cylindrical epithelial cells in continuity with one of the bronchioles. Amniotic cells were also be found elsewhere in the lung parenchyma.

Discussion

To our knowledge, 9 cases have been reported and all save two (King 1938; Gonzalez-Crussi et al. 1980) were newborns or infants with major cranial and CNS abnormalities. The only solitary lesion reported is that of King (1938). The nodules were multiple in the remaining cases reported. It is evident that

the association of this multiple lung lesion with major cranial abnormalities, mainly anencephaly, is a frequent ocurrence, but is not essential.

The histological picture observed in our case showed tubular structures lined by columnar epithelial cells located inside the nodules. These represent bronchioles which penetrate from the adjacent lung parenchyma. The central cavity of the nodules is a bronchial lumen probably dilated by the respiratory movements. The presence of amniotic squamous cells inside these cavities and elsewhere in the lung parenchyma further demonstrates a communication between these cavities and the bronchial tree.

Several hypotheses have been postulated to explain the embryogenesis of this lesion: embolization of brain tissue to the lung (Potter et al. 1942; Potter et al. 1975), aspiration of brain fragments free in the amniotic fluid and faulty migration of neural crest elements to the vicinity of the lung (Kanbour et al. 1979).

The multiple observations of glial and even cerebellar embolism to the lung, usually after traumatic deliveries and other types of cranial trauma (Fobes et al. 1971; Gardiner 1956 and Valdes-Dapena et al. 1967) support the first hypothesis. The appearance of the growth of heterotopic tissue is similar to that of metastases. The meningovascular abnormalities associated with anencephaly and the close relationship with the glial tissue suggest an easy access of neural tissue to the vascular spaces and support the hypothesis of embolization. However, in none of the reported cases intravascular glial tissue could be demonstrated in the lungs. Moreover, the relatively high incidence of traumatic deliveries and of cranial trauma in the general population are in contrast with the rarity of the published cases of glial heterotopy in children and adults. The hypotheses of the aspiration of glial tissue dettached from a malformed brain into the amniotic fluid is more likely to be true if we take into consideration the fact that fetal respiratory movements may contribute to this mechanism.

The possibility of migration of neural tissue to the lung was earlier rejected (Potter et al. 1942) but has been recently recalled (Kanbour et al. 1979). Glial heterotopias are not only found in the lung but they have been also reported in the pharynx, cheek, occiput and scalp. (Lemire et al. 1975, Hevyer et al. 1959). Glial protrusions have also been reported in the subarachnoid space of brain, pons and medulla associated with congenital malformations such the Arnolds Chiari, myelomeningocele and anencephaly and also with more surprising causes such as the fetal alcoholic syndrome (Lemire et al. 1975). Of special interest is the finding of ectopic glial nodules throughout the medulla in an anencephalic fetus (Crome et al. 1955).

The anterior spina bifida seen in our case seems to offer a pathway for the migration of neural cells towards the developing lung. Anterior spina bifida in anencephaly was rare in the serie of Lemire (3,6%) (1978). It may also be found associated to other diseases including neurofibromatosis and neuroenteric cystis (Warkany 1971, Bentley et al. 1960) but its incidence is also low.

The ocurrence of glial heterotopia elsewhere, the more frequent association between heterotopia and congenital malformations and the presence of anterior spina bifida in our case suggest several episodes of neural migration from the central nervous system, reaching the lungs in some cases and favoured perhaps by the presence of anterior spina bifida.

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