Adenomatoid hamartoma of the lung in a neonate

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SYNOPSIS A case of adenomatoid hamartoma in a premature male infant is described and the recent literature is reviewed. The present case demonstrates the frequently associated features of maternal hydramnios of late onset, and premature delivery with foetal respiratory difficulty and anasarca.

The term 'hamartoma' as initially defined by Albrecht (1907) is used to refer to those abnormalities which are of developmental origin, where the tissues have failed to grow along normal lines of differentiation, and are present in abnormal proportions. Occurring in the lung are lesions referred to as 'pulmonary hamartomata' which have been divided on clinical and morphological grounds into two distinct groups.

The first is the so-called chondromatous hamartoma which occurs as a small mass of mesenchymally derived tissue, and is seen only in the adult. Willis (1962) has claimed that these lesions are incorrectly named in that the tumours arise *de novo* in tissues which have reached maturity. They are frequently asymptomatic and are usually an incidental radiological or postmortem finding. Although the chondromatous hamartoma is uncommon, there are several series of case reports, including those of Carlsen and Kiaer (1950) and Adams (1957).

The second group includes those hamartomata in which epithelial elements are dominant, and these were termed 'adenomatoid hamartomata' by Goodyear and Shillitoe (1959). Such lesions are particularly uncommon. Many authors have included adenomatoid hamartomata within the broad classification of congenital cystic disease of the lung. Koontz (1925), in his review of the literature of congenital cystic lesions of the lung, included the report by Stoerk (1897), and other cases where the lesions were undoubtedly of the adenomatoid variety. In addition Willis (1962b) stated that the adenomatoid hamartomata are probably related to congenital cystic disease of the lungs. The first description in English of an adenomatoid hamartoma was by Harris and Schattenberg (1942) who gave an account of two cases of single multicystic pulmonary

tumours in neonates. There have since been at least 18 further cases reported in English, including those of Ch'in and Tang (1949), Jones (1949), Thomas (1949), Graham and Singleton (1955), Craig, Kirkpatrick, and Neuhauser (1956), Gottschalk and Abramson (1957), Bain (1959), Goodyear and Shillitoe (1959), Spector, Claireaux, and Williams (1960), Kwittken and Reiner (1962), Nanson (1962), and Belanger, La Flèche, and Picard (1964).

Ch'in and Tang (1949), in their extensive review of the literature, noted that the first report of a case of a congenital adenomatoid malformation of the lung was by Stoerk (1897), and mentioned 10 other cases which were reported in the German literature between 1905 and 1928. Stoerk (1897), who recognized the adenomatous appearance of the lesion, reported that a pulmonary hamartoma from a neonate was deposited in the Vienna Pathological Institute and described by Karl von Rokitansky about the middle of the nineteenth century.

CASE REPORT

A 27-year-old primigravida presented in the 28th week of pregnancy with acute hydramnios and a rise in blood pressure from previously normal levels to 170/110 mm mercury. Two days after these signs were noted, spontaneous labour began, she was admitted to hospital, and was delivered normally of a male infant weighing 1.07 kg. At birth the child was pink with a pulse rate of 92 per minute, but with flaccid muscle tone and marked oedema affecting the head, face, and abdomen. Only a few spasmodic attempts were made to breathe.

For 35 minutes after birth intermittent positive pressure respiration was carried out, after which spontaneous respiration started but lasted only for 30 minutes. Resuscitation was again attempted but spontaneous respiration was not established. The infant was therefore transferred by ambulance to a neonatal intensive care unit, respiration being maintained during the three-hour

journey by continuous intermittent positive pressure respiration. During the transfer the heart stopped, but the heart beat recommenced following external cardiac massage. On arrival at the intensive care unit six hours after birth the infant was moribund and acidotic with severe carbon dioxide retention. Despite attempts at resuscitation for a further three and a half hours, there was no spontaneous respiration and death followed a second cardiac arrest nine and a half hours after birth.

Postmortem examination showed a small male infant measuring 36 cm from crown to heel, and 24 cm from crown to rump. There was marked oedema of the face and scalp, and of the anterior abdominal wall. On opening the thoracic cavity a large white mass was seen which appeared to fill almost the whole of the thorax. This mass measured 6.5 cm in length by 3.5 cm in breadth and 4.0 cm in depth, weighed approximately 50 g, and caused displacement of the mediastinum, heart, and great vessels to the left (Fig. 1). The apex of the heart lay against the left lateral wall of the thorax.

The surface of the mass was smooth but firm irregularities were palpable within, giving the impression of lobulation. It arose from the inferior and anterior surfaces of the upper lobe of the right lung. The middle and lower lobes showed no anatomical abnormality but the only expanded area was in the lower lobe. The tumour and the remainder of the right upper lobe were covered by a single continuous layer of visceral pleura, although the tumour and adjacent lung tissue were distinct and adherent only by way of a thin fascial layer of connective tissue.

The trachea was normal, as were the two main bronchi and the bronchi to the middle and lower lobes of the right lung. The right upper lobe bronchus became atretic shortly beyond its origin and continued as numerous fibrous strands each of which entered the tumour mass at a different point after coursing through the fascial layer beneath the pleura and between the lobes of the tumour. The branch of the pulmonary artery to the right upper lobe similarly divided and ramified widely as subpleural vessels (Fig. 2). None of the branches of these vessels were seen to penetrate the mass directly, but divided into minute subdivisions on its surface.

On section the mass had a whitish, lobulated appearance and contained multiple cysts which measured up to 1.5 cm in diameter (Fig. 1). Microscopic examination of these cystic spaces showed bronchial and bronchiolar-like structures with a varying degree of dilatation (Fig. 3). The epithelial lining of these 'bronchioles' showed numerous papilliferous processes extending into the lumen, covered by a single layer of cuboidal or columnar cells which in some cases appeared ciliated (Fig. 4). In the larger air spaces the epithelium was stratified. These cystic spaces were surrounded by a layer of elastic tissue which was more prominent about the larger cysts. Collagen was also seen surrounding the large cystic structures but not elsewhere. Among the epithelial lining cells were sparse clumps of mucin-secreting goblet cells clearly demonstrated by alcian-blue and periodic-acid-Schiff staining techniques (Fig. 5).

Near the periphery of the mass the bronchiolar-like structures gave way to formations resembling foetal alveoli. These alveoli were dilated, lined by a low cuboidal

FIG. 1. Coronal section of adenomatoid hamartoma demonstrating multicystic nature and relationship to abdominal organs.

FIG. 2. Posterior aspect of adenomatoid hamartoma on the right with aorta and lower lobe of right lung on the left. The pulmonary artery to the hamartoma crosses the pointer with the right lower lobe bronchus to the left.

FIG. 3. Adenomatoid hamartoma of lung. Papillary epithelial processes within large air passages and adjacent bronchiolar-like structures. Alveolar formation at the extreme right. Haematoxylin and eosin $\times 36$.

or flattened epithelium, and their abnormally thick walls contained numerous capillaries. The alveolar-like structures were best seen immediately beneath the pleura, but occurred infrequently throughout the remainder of the mass where they were small in number in comparison with the dilated, tortuous air passages (Fig. 4).

Prominent strands of smooth muscle were seen throughout the tumour mass, but cartilage was not present. There were no large blood vessels within the mass, although capillaries and arterioles were prominent immediately beneath the mucosal layers.

The hamartoma thus consisted of abnormal bronchial and bronchiolar-like structures embedded in a mixed

connective tissue stroma, without cartilage or demonstrable bronchial communication. The left lung was shown to be atelectatic but otherwise normal, and the placenta was not available for examination. No abnormality was found in any other organ.

DISCUSSION

Of the ten cases reviewed by Ch'in and Tang (1949), two were associated with maternal hydrops, while anasarca was present in nine. The lesion was present in one lobe or part of a lobe in six of these

FIG. 4. Subpleural alveolar structures on the left with cuboidal and flattened lining epithelium. Strands of smooth muscle between the smaller air passages. Haematoxylin and eosin $\times 110$.

FIG. 5. Clump of columnar mucus-secreting cells within a small bronchial structure. Mucus is seen as a dark layer on the surface of the epithelial cells. Alcian blue $\times 360$.

10 infants. Several authors have commented on the absence of arteries within the hamartoma, and on the absence of normal mucin-secreting cells in the epithelium. A gastric-like epithelium was seen in some of the polypoid epithelial malformations.

Of seven of the more recently reported cases (Ch'in and Tang, 1949; Jones, 1949; Thomas, 1949; Graham and Singleton, 1955; Bain, 1959; Goodyear and Shillitoe, 1959; Spector *et al*, 1960; and the present case), six presented with maternal hydramnios and in three of these infants anasarca was present. Six of the seven were premature, mostly by about 12 weeks. Five of the seven were born alive, four of these dying within one hour of birth, and one within 10 hours. The gross appearance of the tumour was similar in five of the six cases, while the essential histological feature was the disorganized overgrowth of bronchiolar-like structures, lined by a simple columnar or cuboidal epithelium and embedded in varying amounts of connective tissue. Small amounts of cartilage were present in one instance (Jones, 1949) and mucus-secreting cells in three others. The hamartoma arose from one lobe of the lung in seven cases, and from the whole lung in the remaining one.

Another 10 cases have been described by Graham and Singleton (1955), Craig *et al* (1956), Gottschalk and Abramson (1957), Kwittken and Reiner (1962), and Nanson (1962) which differed from those above either in their appearance or mode of presentation. Nine of these were diagnosed some time after birth, usually after the onset of cyanosis or other respiratory symptoms. Maternal hydramnios and foetal anasarca were present only in the case of Gottschalk and Abramson which was stillborn. The first case of Kwittken and Reiner (1962) was unusual in that arteries were found within the hamartoma and alveoli were seen throughout the malformation as in the case of Belanger *et al* (1964). Abnormal mucus-secreting cells were found in six of the eight cases. Five cases survived operation and were those of Graham and Singleton (1955), Craig *et al* (1956), and Nanson (1962).

Craig *et al* (1956), Bain (1959), and Kwittken and Reiner (1962) have listed characteristics which they considered differentiated the adenomatoid malformation from cystic disease of the lung. These features included the absence of bronchial cartilage, the presence of abnormal mucus-secreting cells, and marked proliferation of terminal bronchiolar structures with alveolar differentiation only in the immediate subpleural region.

The case of Gottschalk and Abramson (1957), although described as adenomatoid, contained cartilage and had a gross appearance unlike that of a typical adenomatoid hamartoma. The only other

hamartoma containing cartilage was that of Jones (1949) where the lesion was almost completely solid and did not have a cystic appearance.

Craig *et al* (1956) also pointed out that a number of apparently simple cysts of the lung contained hamartomatous areas. However, in the majority of cases it is possible to classify the disorder either as an adenomatoid hamartoma or as uncomplicated cystic disease of the lung. It has generally been concluded that the anasarca arises directly as a result of mechanical interference with the circulation, and the appearance in this case would support the hypothesis.

The frequency of maternal hydramnios in association with foetal adenomatoid hamartoma is of interest. It has long been known that atresia of the upper part of the foetal gastrointestinal tract is frequently associated with acute maternal hydramnios (Lloyd and Clatworthy, 1958; Jeffcoate and Scott, 1959). Amniotic fluid is thought to be reabsorbed in the upper portion of the foetal alimentary tract and returned to the maternal circulation by way of the placenta. This mechanism was considered important by Jeffcoate and Scott (1959), who suggested that absorption by the foetal lungs may play a lesser part in the resorption of amniotic fluid. They disagreed with Plentl and Gray (1957) who demonstrated experimentally that foetal swallowing played a minor part in the removal of amniotic fluid in hydramnios.

It is possible that oesophageal atresias which totally obstruct the alimentary tract, major abnormalities such as anencephaly which interfere with swallowing, and intrathoracic space-occupying lesions, including pulmonary hamartomata and oesophageal haemangiomas (Fraser, 1968), may cause the accumulation of amniotic fluid with the development of hydramnios. However, the absence of antidiuretic hormone in the anencephalic foetus (Benirschke and McKay, 1953) may contribute to the formation of hydramnios. Other pulmonary lesions have also been associated with hydramnios. Bates (1965) noted the association of severe hydramnios with bilateral pulmonary hypoplasia in three cases and proposed that increased capillary pressure within the lung could enhance the 'normal intrapulmonary ultrafiltration' process and formation of amniotic fluid. More probably, the amount of fluid resorbed by the hypoplastic lung is reduced. Charles (1960) described a case of nasopharyngeal teratoma with pulmonary glial deposits associated with hydramnios where he attributed the latter to the impaired pulmonary resorption of amniotic fluid.

Ch'in and Tang (1949), Thomas (1949), and Spector *et al* (1960) regarded the malformation as

being related to congenital cystic disease of the lung, to which it does bear some structural resemblance. Simple lung cysts of apparently congenital origin are relatively common, but the adenomatoid hamartoma must be almost as frequent a cause of respiratory difficulty in the neonate. Of the 108 cases of congenital cystic lesions of the lung reviewed by Koontz (1925), only 15 occurred in stillbirths or in infants who died shortly after birth. Similarly, only 36 of the 318 cases of lung cysts in children reviewed by Schenck (1937) were diagnosed at birth. At least a few of these cases appear to have been adenomatoid hamartomata.

The respiratory difficulty must in many cases be attributed to compression of the remaining normal lung, and not to the expanding lung syndrome described by Spector *et al* (1960), as in four of 11 cases where this symptom was noted there was no demonstrable bronchial communication with the malformation. Furthermore, the hamartoma must in many cases have attained a considerable size *in utero* to account for the presence of foetal anasarca and hypoplasia of the contralateral lung.

It is not contested that both simple cysts and adenomatoid hamartomata are of congenital origin. However, Willis (1962c) states that the term 'hamartoma' should be used where there is clearly an underlying developmental anomaly with excess of one or more of the tissue components.

There seems no doubt of the hamartomatous nature of this condition with its abnormal proliferation of the pulmonary tissues, when compared with congenital cystic disease of the lung, where the lesion appears to be a structural defect in the development of the air passages and where the various tissues are present in normal proportions. It is suggested that the term 'adenomatoid hamartoma' of the lung, as suggested by Goodyear and Shillitoe (1959), is preferable to that of 'congenital cystic adenomatoid malformation' as being less likely to

cause confusion until there is a better understanding of the origin of these two conditions.

The association of maternal hydramnios and premature delivery with foetal anasarca and respiratory difficulty suggests the presence of an intrathoracic mass, provided that haemolytic disease of the newborn can be excluded.

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