Bronchopulmonary moniliasis in the newborn

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SYNOPSIS Ten instances of bronchopulmonary moniliasis due to *C. albicans* in neonatal infants 1 to 11 days of age, are described. The incidence was 1.05% out of a total of 947 consecutive necropsies on neonates. Diagnosis was established by morphological identification of the fungi. Seven cases were associated with inflammatory exudation. In three cases inflammation was absent. Infection secondary to monilial vaginitis in the mother appears to have been over-emphasized. The more common mechanism appears to be aspiration after delivery.

Although moniliasis of the mouth, larynx, oesophagus, and gastrointestinal tract in infants is well known, its occurrence in the lungs is a distinctly rare finding in the immediate neonatal period. The only references we have been able to find are those of Birch-Hirschfeld (1875, cited by Dobias, 1957), Vorreith (1953), and Hottinger (1956) who each reported single cases. The pulmonary lesion was secondary to monilial sepsis and thus differs from the subject of the present study. Nézelof and Sarraut (1957) listed a case of isolated monilial pneumonia that is similar to ours. Ludlam and Henderson (1942) mention the occurrence of pulmonary moniliasis in the neonatal infant, but no details are given. Consequently a report appears warranted of 10 instances of bronchopulmonary moniliasis in neonates due to *C. albicans*.

MATERIAL AND METHODS

A neonate for the purpose of this study is defined as a newborn infant up to the age of 10 days. During the period of observation a combined total of 947 neonates was necropsied. Lung tissues for histological study were routinely stained with haematoxylin-eosin, supplemented by Gram and P.A.S. staining, and, in a few instances, by staining with Gomori's hexamethylenetetramine reagent. Bronchial swabs for cultivation were taken in two cases and inoculated on Sabouraud media.

RESULTS

The age, sex, birth weight and length, therapy, and summary of pathological findings are listed in Table I. Ten instances of bronchopulmonary moniliasis were discovered, representing an incidence of

1.05%. Two infants, aged 11 days, have also been included in the series. The sexes were evenly distributed. The youngest newborn was 1 day of age. Delivery was by caesarean section in one case (no. 2). Deliveries were in all cases performed in a maternity ward, and the infants were under institutional care until the time of death. When present, clinical signs pointing to respiratory complication (cyanosis, temperature, and tachypnoea) appeared, on the average, on the sixth day after delivery. Positive cultures of *C. albicans* were not obtained from any case.

GROSS FINDINGS

In cases 1, 8, 9, and 10 the lungs were not characteristic in any way but merely showed patchy areas of atelectasis. In the remaining neonates the paravertebral areas exhibited focal or diffuse consolidation of varying degree. To the naked eye the lung parenchyma presented numerous dark red areas with small yellow nodules about 2 to 5 mm. in diameter, and somewhat soft in consistency. Liquefaction was visible in the centre of some of the nodules. In two instances the overlying pleura was covered with fibrin, and in one the pleural cavity contained purulent exudate. The large bronchi were generally normal in appearance. Occasionally they were filled with a viscous liquid, light brown or pale yellow colour.

HISTOLOGY

Two distinct groups were noted, one with and the other without an inflammatory reaction. In the former group (cases 1 to 7) large areas of alveoli and

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TABLE I

SUMMARY OF CLINICAL DATA, THERAPY, AND PATHOLOGICAL FINDINGS

No.	Weight (g.)	Length (cm.)	Sex	Age (days)	First Clinical Signs (day after delivery)	Antibiotics	Localization	Bacteria	Aspiration	Other Pathological Findings
1	2,050	47	F	4	—	Penicillin	Lungs	Gram — bacilli	—	Haemotorachis, diffused renal necrosis
2	2,600	44	M	6	2	Streptomycin Penicillin	Lungs	Gram — bacilli	Milk Vernix	—
3	2,600	52	F	10	5	Streptomycin Aureomycin Penicillin	Pharynx Oesophagus Lungs	Gram + cocci	Vegetable particles	Thrombosis of ductus arteriosus, enterocolitis, otitis media, slight nephrosis with calcification
4	2,850	50	M	11	10	Terramycin Penicillin	Oral cavity Larynx Pharynx	Gram + cocci	Vegetable particles	Otitis media
5	2,350	46	M	7	—	Aureomycin Terramycin Penicillin	Lungs Stools Oral cavity Oesophagus Lungs	Gram + cocci and bacilli	Vernix	—
6	2,300	50	F	11	8	Penicillin Streptomycin Erythromycin	Lungs	Gram + cocci	Vegetable particles	Ebstein malformation of tricuspidal valve, labile and palatal cleft
7	2,650	47	M	7	6	Neomycin Erythromycin Penicillin	Lungs	Gram + cocci	—	—
8	1,000	27	M	9	—	Penicillin Erythromycin	Lungs	Gram + bacilli	Vernix	Gastroenterocolitis, pulmonary haemorrhage
9	1,000	34	F	4	—	—	Lungs	Gram — bacilli	Vernix	—
10	2,400	49	F	1	—	Penicillin	Lungs	—	—	Pulmonary hyaline membranes

bronchi were consolidated by a cellular exudate consisting predominantly of polymorph leucocytes in which masses of blastospores and pseudomycelia of *C. albicans* were present mixed with the inflammatory cells (Figs. 1 and 2). Rarely, the lumina of blood vessels were plugged with organisms. As a rule, pseudomycelia could be seen penetrating the broncholar wall into the adjacent lung parenchyma. The epithelial lining of the bronchioles showed occasional focal squamous metaplasia. The inter-alveolar septa were hyperaemic, and, in spots, necrotic or indistinct. Interstitial as well as intra-alveolar haemorrhages were present, particularly in the vicinity of the inflammatory exudate.

Generally, oedema and focally distributed collapse and emphysema were found in one or more areas of all the lung sections. The epithelium of some of the alveoli was hyperplastic. An additional feature in two cases was the finding of a bright yellow material, quite abundant in certain areas, in the bronchi and alveoli. It was identified as bilirubin with Fouchet's reagent (Hall, 1960). In one instance a few scattered giant cells were seen phagocytosing blastospores and, rarely, pseudomycelia (Fig. 3). In two cases the bronchi and bronchioli were filled with quantities of particles, most probably of vegetable origin (Fig. 4), closely associated with the mycotic flora (Fig. 5).

In the second group (cases 8 to 10), in which there was no inflammatory reaction, *Candida* varied considerably in number. In case 10 they occurred as dis-

crete, isolated forms in a few bronchioli. In the other two cases they were present as more abundant growths in the bronchioli as well as in a few alveoli. The lung parenchyma was for the most part atelectatic with foci of intra-alveolar haemorrhages. In case 8 a number of bronchioli contained particles identical to those described above.

In the majority of cases in both groups *C. albicans* was found, mainly in the form of blastospores. The intermingled pseudomycelia when present were distinctive and were easily identified (Fig. 6). Except in cases 1, 7, and 10, aspirated vernix squames, milk, and vegetable particles were found in one form or another in all the lungs but *Candida* only in the vegetable particles. Bacteria in varying numbers were identified morphologically in all instances except in case 10.

An incidental finding was the small foci of necrosis and leucocytic infiltration in the renal medulla in case 1. Gram, P.A.S., and polychrome blue staining did not disclose *Candida* or any other infectious organism.

Candida were seen in cases 3, 4, and 5 in sites other than the lung.

DISCUSSION

Judging by the bronchial propagation of the fungi, it is clear that the portal of entry in our series of cases was the upper respiratory tract. Hence, moniliasis

FIG. 1. The bronchi are choked with blastospores of *Candida*. P.A.S. $\times 64$.

FIG. 2. Masses of *Candida* in alveolar exudate. Gram $\times 525$.

FIG. 3. Alveolar leucocytic exudate containing a multinucleated giant cell. Haematoxylin-eosin. $\times 455$.

FIG. 4. Bronchi filled with aspirated vegetable matter. A rim of *Candida* surrounds a particle in the middle right field. Haematoxylin-eosin. $\times 128$.

FIG. 6. High-power view of the mycotic flora in an alveolus showing blastospores and pseudomycelia. The septate character of the fungi is evident. P.A.S. $\times 1,152$.

FIG. 5. Detail of Fig. 4 showing blastospores around a particle. Haematoxylin-eosin. $\times 616$.

where associated with inflammation is, properly speaking, aspiration pneumonia. Epstein (1924) found oral thrush in 2.4% neonates and in 24.6% neonates and infants 6 days to 1 year of age.

The exogenous source of aspirated *Candida* is the controversial point. Generally, aspiration from maternal vaginal infection during passage of the foetus has been greatly emphasized (see Dobias, 1957, for review). Studies on this problem are conflicting. Woodruff and Hesselstine (1938) state that in a child born of a mother with vaginal moniliasis the chances of acquiring the infection are 35 times greater than in a child of a healthy mother. Others (Štastná, Drexler, and Hnátek, 1956) give a lower figure, and some writers (Ludlam and Henderson, 1942) go so far as to claim that maternal vaginitis is practically without importance for the infant. Undoubtedly bronchopulmonary moniliasis secondary to vaginal infection in the mother may be possible but the results in the present series do not suggest a vaginal source of infection. All except one of the neonates were 4 days or older. If infection is acquired during birth, it seems likely that moniliasis would have been more frequently observed in younger infants. In one instance delivery was by caesarean section, thus excluding the likelihood of vaginal contamination. In case 9 the twin brother died two days after birth from hyaline membranes and suffocation, without evidence of *Candida*. In cases 3, 4, and 6 the fungi were in definite association with aspirated food particles. In cases 1, 2, and 10 the possibility of vaginal infection cannot be entirely dismissed, although definite evidence for or against is lacking.

In view of the ubiquitous nature of *C. albicans* the sources of infection are many. Clothes, bed sheets, and rubber teats, to mention but a few objects, are potential sources of fungi. Stowens (1959) also mentions the danger of infection from the nipples of the mother.

In three instances monilia were clearly disseminated from the mouth to the pharynx and larynx. In the remaining cases it is conceivable that a primary lesion in the mouth or pharynx was so small as to have been missed at necropsy. References to this possibility have been reported in the literature (Ludlam and Henderson, 1942; Vorreith, 1953).

The occurrence of *Candida* in the bronchi without

evoking an inflammatory reaction appears to point to the very early stages where, although the pathogenic organisms are present, proper conditions in the host are lacking for full expression of virulence. An inflammatory reaction to *Candida* in the oral mucosa, for example, is generally slight. To reason by analogy, lesions elsewhere might very well begin with extremely minimal exudation or none at all. Furthermore, it is highly probable that the period of latency is often related to the administration of antibiotics.

The presence of bacteria together with *Candida* raises the question as to whether the former and not the latter was the aetiological agent of the pneumonia. The sheer massiveness of *Candida* compared with the bacterial flora seems to make this possibility unlikely. Moreover, *Candida* was always found close to the foci of severest inflammation.

Provided that sections are properly stained there is little difficulty in identifying the fungi. Ordinary haematoxylin-eosin stains *Candida*, but it is not recommended for unequivocal identification as the blastospores can often be mistaken for disintegrated nuclear fragments of leucocytes or vice versa. In two instances where a presumptive diagnosis of monilial pneumonia was considered at necropsy, bronchial swabs failed to produce growths. Equally surprising is the fact that in other cases of positive cultures (not included in the present report) no organisms were found histologically. Aside from the possibility that this may represent accidental contamination, no explanation can be offered at the present time.

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