Adrenal changes in chorioamnionitis

In a review of cases of Candida chorioamnionitis, Lopez and Aterman (1968) emphasized that 6 of the 9 cases in published reports were born before 38 weeks' gestation. In a subsequent report, Ho and Aterman (1970) reported a further case of Candida chorioamnionitis in a spontaneous abortus of 14 weeks' gestation, and they postulated that chorioamnionitis could initiate premature labour and abortion. Recent experience with a small series of cases of chorioamnionitis prompted this report since the findings in the adrenal glands appeared compatible with such a hypothesis.

Case reports

Within a space of 6 weeks, 4 immature stillborn infants, all suffering from chorioamnionitis, were examined at McMaster University Medical Centre. The main clinical features are outlined in the Table. It should be pointed out that in the Province of Ontario, Canada, the lower limit of viability is set at 20 weeks' gestation, in distinction to the limit of 28 weeks in the United Kingdom.

In all cases there was histological evidence of a severe congenital pneumonia, and in those cases where the middle ear was examined, otitis media with a characteristic mixed interstitial inflammatory response and luminal exudate in both sites. In Case 3 there was evidence of septic pulmonary venous thrombi and a fibrinous pleuritis, and in Cases 3 and 4 evidence of disseminated capillary thrombi in liver, adrenals, pituitary, kidney, and spleen. Intraventricular bleeding was seen in Case 1, while subependymal haematoma were found in Cases 2 and 4; subcapsular hepatic haemorrhage was noted in Cases 2 and 4. Bowel ischaemia was noted in Cases 3 and 4.

Changes in adrenal glands. The glands were weighed after fixation. While normal values for organ weights in infants of extreme immaturity are not readily available, the size of the glands did not appear to differ markedly from those of other stillbirths of comparable gestation not suffering from chorioamnionitis. The glands were dark brown in colour and examination of the cut surface revealed obvious and considerable depletion of cortical lipid. Histologically, the impression of lipid depletion was confirmed, with the additional finding of considerable cytoplastic degeneration in the fetal and definitive cortex. This produced an extremely pronounced pseudotubular or follicular appearance, often with haemorrhage into the lumina (Fig.). The lumina contained scattered fibrinous aggregates with nuclear debris, red cells, and eosinophilic (presumably proteinaceous) fluid. In the 2 infants where segmental

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Gestation (wk)</th>
<th>Birthweight (g)</th>
<th>Obstetric features</th>
<th>Organism</th>
<th>Findings other than chorioamnionitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>25</td>
<td>750</td>
<td>Intrauterine contraceptive device with known Candida albicans in vagina</td>
<td>C. albicans</td>
<td>Funisitis; congenital pneumonia; otitis media; yeast in gastrointestinal tract; intraventricular haemorrhage</td>
</tr>
<tr>
<td>2</td>
<td>23</td>
<td>370</td>
<td>Leaking membranes over a week; antepartum haemorrhage</td>
<td>Unknown</td>
<td>Congenital pneumonia; unilateral segmental necrosis of adrenal; subependymal haematoma; subcapsular hepatic haematoma</td>
</tr>
<tr>
<td>3</td>
<td>33</td>
<td>1800</td>
<td>Group B, β-haemolytic streptococcus in maternal blood and vaginal swab; membranes ruptured 48 hr; pronounced slowing of fetal heart</td>
<td>Group B, β-haemolytic streptococcus</td>
<td>Early meningitis with dense cellular infiltrate in subarachnoid space; congenital pneumonia, pleuritis; otitis media; pulmonary venous thrombi and disseminated capillary thrombi; mucosal ischaemia of small bowel</td>
</tr>
<tr>
<td>4</td>
<td>26</td>
<td>600</td>
<td>Membranes ruptured 48 hr; antepartum haemorrhage; prolapsed cord</td>
<td>Haemophilus influenzae</td>
<td>Early meningitis with dense cellular infiltrate in subarachnoid space; congenital pneumonia; otitis media; segmental necrosis of adrenal; disseminated capillary thrombi, subependymal haematoma; subependymal haematoma; mucosal ischaemia of large bowel</td>
</tr>
</tbody>
</table>
FIG. (a) A normal adrenal gland is shown, and abundant lipid present is responsible for the pallor of the cytoplasm in contrast to (b) a representative area of the adrenal cortex in Case 3 showing extensive degeneration of the superficial areas of the definitive cortex with the production of a typical follicular or pseudotubular appearance. Note the 'compact' cytoplasm of the fetal cortex indicative of lipid depletion. (Haematoxylin and eosin. ×622.)
adrenal necrosis was present, the necrotic areas appeared to merge with the tubular areas, and the necrosis was of the liquefactive variety with haematoema formation.

The changes seen in routine preparations in these cases are those of a severe and prolonged 'stress reaction' in the fetal adrenal, and are comparable to those seen in adults in the acute, active phase of such a state (Symington, 1969).

In all 4 cases the thymus showed moderate depletion of cortical lymphocytes, compatible with a stress reaction.

Discussion

The thymic and adrenal changes seen in this small series of cases suggest that the fetal adrenal cortex responded to the stress imposed by an intrauterine infection. Changes that are extremely similar are seen in the adrenal glands at necropsy in many infants dying from various causes, and Stowens (1966) described the lesion in association with prolonged infections, severe metabolic derangements, and in premature infants. He used the term 'functional exhaustion' to describe its significance. It is reasonable to suggest, therefore, that the appearances of the adrenal gland in the present series suggest an active outpouring of adrenal steroids. Since all these infants were stillborn it is obvious that this reaction must have occurred in utero, and problems of postnatal adjustment could not have contributed to the appearances seen.

The widely known work of Liggins (1969) in inducing labour in sheep by the infusion of steroids to the fetus makes it likely that in the present series labour was initiated by an outpouring of steroids from the stressed adrenal, a finding in keeping with the hypothesis of Ho and Aterman (1970). It is unfortunate that in the reports published on chorioamnionitis the adrenal glands are not described in detail, though it should be possible to review the findings.

The adrenal changes raise certain other issues of potential interest. The relation of pseudotubular zones to the necrotic lacunar foci, described by deSa and Nicholls (1972), needs to be assessed since the lacunar lesion, believed to be the central lesion of haematoema formation in the adrenal glands of perinatal infants, may well be dependent on the coexistence of a severe stress reaction in an otherwise ischaemic gland.

The effects of such an outpouring of steroids on the development of the surfactant system of the lung (Kotas and Avery, 1971) need to be considered as well, and it appears that the infants with chorioamnionitis offer a naturally-occurring population in which this problem could be studied.

Short reports

The finding of otitis media in these stillborn infants is in keeping with the findings of Benner (1940), but represents a very different pathogenesis from that described in a population of infants with otitis media, where chorioamnionitis was extremely uncommon (deSa, 1973).

Summary

Changes in the adrenal glands of 4 immature stillbirths with chorioamnionitis due to several different micro-organisms are described. These changes are interpreted as being consistent with a severe stress reaction, and it is suggested that the output of steroids in utero by the fetus initiated labour.

References

deSa, D. J. (1973). Infection and amniotic aspiration of the middle ear in stillbirths and neonatal deaths. Archives of Disease in Childhood, 48, 872.
Williams and Wilkins, Baltimore.

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Neonatal hypoglycaemia with congenital malformation of pancreatic islets

Neonatal hypoglycaemia is frequently associated with dysmaturity and is rarely the result of congenital abnormalities of the pancreatic islets (Grant and Barbor, 1970). These diagnoses should be considered in refractory or prolonged neonatal hypoglycaemia, and exploratory laparotomy has been suggested when symptomatic hypoglycaemia extends past the second week of life (Robinson et al., 1971). We report such a case with unusual islet pathology.
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