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Case report

Foamy degeneration of placenta

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Summary. A case of striking foamy transformation of placental and stromal decidual cells is reported. These findings are similar to those described in the placenta of infants affected by fetal storage disorders.

However, in our case a very critical study allowed us to conclude that these changes were non-specific and regressive. They were presumed to be concomitant with fetal death or possibly secondary to oedema or anoxia.

This case is reported to demonstrate how difficult the differential diagnosis of the appearance of the placenta in fetal storage disorders may be.

Key words: Placenta pathology – Placental disorders, pathology – Xanthomatosis – Cell membrane permeability

In 1976 Powell et al. described four cases of foamy changes in placental cells which were secondary to fetal storage disorders. One of those cases was eventually diagnosed as I-Cell disease. A similar placental involvement in a case of G_{M1}-gangliosidosis resulting in foamy appearance of syncytiotrophoblast was reported by Lowden et al. (1973). The possibility that examination of villi will give clues to inborn errors of metabolism has been stressed by Altshuler (1981).

Several years ago, we had the opportunity to examine a placenta which showed a striking foamy appearance of syncytiotrophoblastic and villous stromal cells, thereby assuming features similar to those described in fetal storage disorders. A detailed and critical study of this case allowed us to ascertain that such a foamy appearance was the result of degenerative non-specific changes sustained by intense oedema or perhaps secondary to fetal death.

Our case is extremely unusual and is reported not for its pathological significance, which is limited, but for its noteworthy diagnostic relevance.

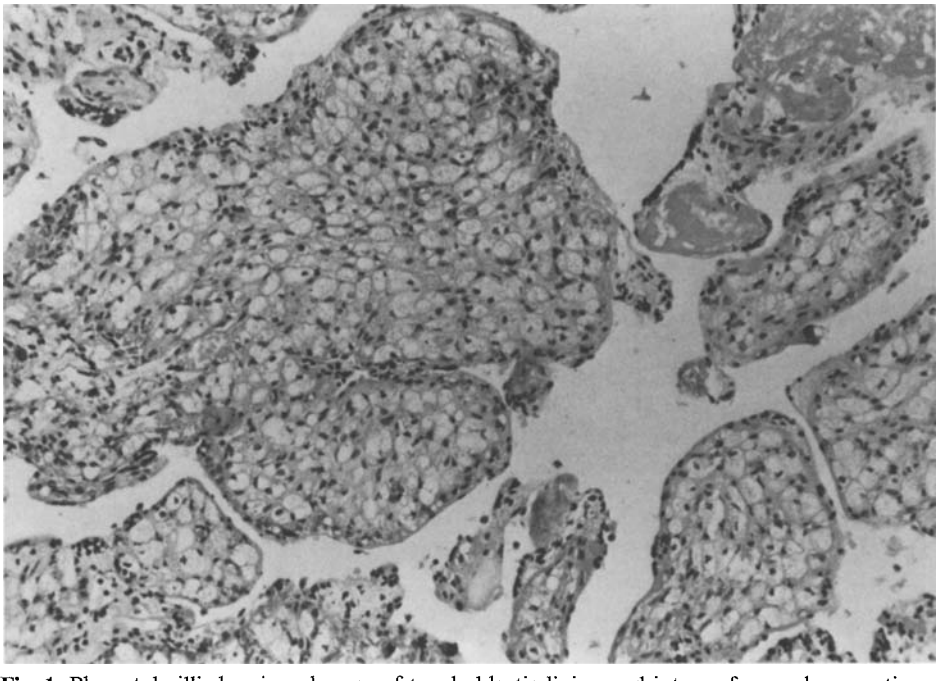

Fig. 1. Placental villi showing absence of trophoblastic lining and intense foamy degeneration of stromal cells. Haematoxylin-eosin, × 40

Case report

A young primipara was seen at Gaslini Institute Children's and Women's Hospital in 1978 for two episodes of metrorrhagia during pregnancy. Her past clinical history was unremarkable. An excessive increase of body weight was recorded during pregnancy. Measurements of blood urea, glucose and blood pressure were within normal values. A spontaneous premature labour resulted in the birth of a 3,100 g infant with evidence of massive anasarca and cardiorespiratory distress. The infant died 2 days later in spite of resuscitation and intense medical therapy.

Autopsy revealed the absence of congenital malformations and striking anasarca of unknown aetiology, which could not be related to Rh, ABO or MEN incompatibility. The renal vessels were small but otherwise unremarkable. Histology revealed pulmonary atelectasia and hyaline membrane disease. The placenta was not examined.

In 1979 the patient again became pregnant. A duodenal ulcer had been radiographically diagnosed prior to the pregnancy. The glucose curve was within normal limits. At the fifth month of pregnancy amniocentesis yielded a brown coloured liquid, followed soon thereafter by intrauterine fetal death. Labour was induced revealing an extremely macerated immature male conceptus. The autopsy was not contributory due to intense post-mortem autolysis. The time interval between fetal death and placental expulsion was calculated to be about 2–3 days. Leucocyte lysosome enzyme measurements including fucosidosis, β-galattosidasis, α-mannosidasis, β-esosaminidasis, neuraminidasis were performed in both the patient and the husband all of which resulted in normal limits.

Pathological findings

The placenta under study was related to the second pregnancy. Only a part of it was delivered to the laboratory and did not reveal any significant macroscopic anomaly. Histologically,

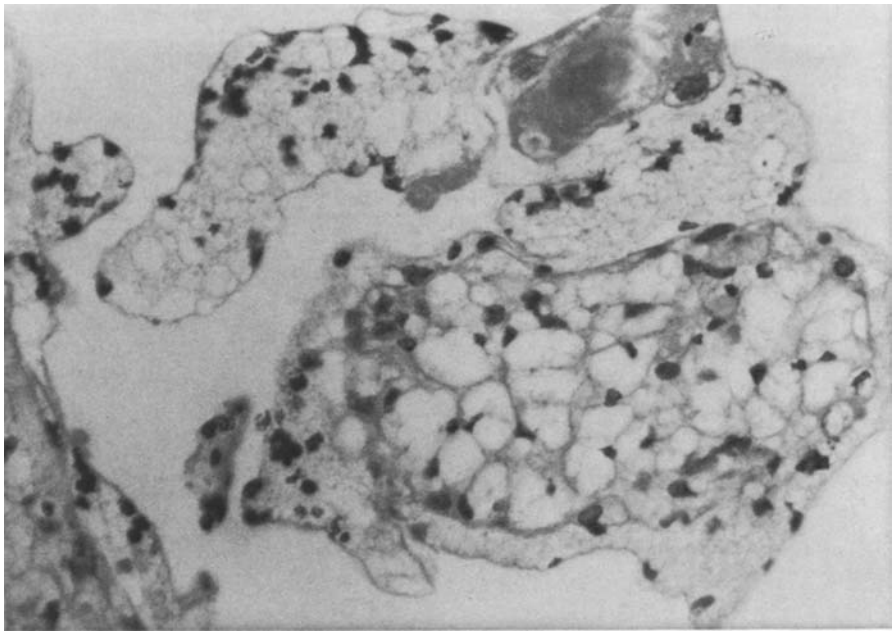

Fig. 2. Another villus showing foamy appearance of both stromal cells and syncytiotrophoblast. Note small pyknotic nuclei in the latter. Haematoxylin-eosin, ×400

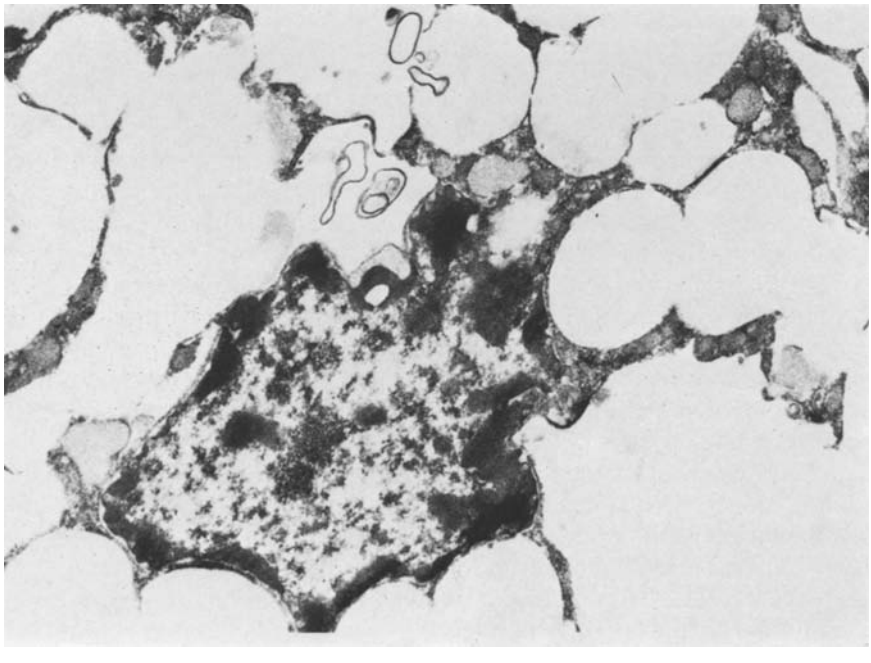

Fig. 3. Ultrastructural features of the foamy cells. Numerous round confluent vacuoles with clear fluid content fill the cytoplasm and compress the nucleus. ×7,000

the villi revealed a striking foamy appearance of syncytiotrophoblast and stromal Hofbauer cells (Figs. 1 and 2). The vacuoles were small, of even size, and produced notches on the nuclei. The villus stroma was packed with foam cells in a mosaic like pattern. The reticulin stain disclosed encircling of any single stromal cell by argyrophilic fibrils. Another important finding was the distinctly necrotic appearance of the syncytiotrophoblast which was frequently lacking or detached from the villus surface (Figs. 1 and 2). The nuclei of the syncytiotrophoblast and stromal cells were intensely affected by pyknosis and karyorrhexis. Numerous calcium salt deposits and calcospherites were scattered inside the stroma and in the syncytiotrophoblast resulting in marked dystrophic calcification.

In several marginal areas the foam appearance was less pronounced, whereas intense stromal oedema gave the villi the usual appearance of hydropic or molar degeneration. Cytotrophoblast cells were scanty and scattered under the syncytiotrophoblast. The chorionic vessels were arteriosclerotic. Intervillous fibrinoid degeneration was a frequent finding. Syncytial knots were not found. An additional important characteristic of the placenta was the fine foamy appearance of stromal decidual cells. The vacuole content was repeatedly negative to the following stains: Sudan for neutral lipids, PAS, Best for glycogen, alcian blue at pH 1.2, 1.5, 2.1, Giemsa and toluidin blue. The Von Kossa stain underlined the mineral nature of the concretions.

A general impressive finding was the cellular enlargement either of trophoblast or Hofbauer cells which clearly suggested an increase of fluid cellular content.

The ultrastructural investigation of placental fragments revealed that the Hofbauer cell and syncytiotrophoblast cytoplasm was packed with round and confluent vesicles of uniform size which totally replaced and obliterated any cytoplasmatic structure (Fig. 3). The vesicle content was clear, watery and structureless (Fig. 3). Some vesicles were membrane-bound. The nuclei were pyknotic and compressed by the vesicles which caused crescentic notches on their surface. Dehiscent cytoplasmatic organelles were scattered in some vesicles. Single cell elements contained a single huge vacuole which displaced the nucleus.

Discussion

The foamy appearance of placental cells in the present case has a striking similarity to the findings previously observed in the placenta of children affected by storage disorders. However, it can be convincingly demonstrated that the foamy changes in our case is a non-specific degenerative transformation which is probably secondary to oedema or perhaps to fetal death.

Fox has stated that after 15 h of fetal death the causative factors of fetal death cannot be determined by the placental findings (1978). Therefore we can conclude that the findings in our case are probably artefactual.

The complete negativity of all the histochemical investigations clearly indicates that the stored material is water. The necrotic appearance of syncytiotrophoblast has demonstrated the regressive and degenerative nature of the process involving the placenta. The negative results of parental tests for possible carrier status confirm our assumption. Another important confirmatory sign is given by the foamy vacuolization of decidual stromal cells, a finding in contrast to congenital storage disease as reported in their cases by Powell et al. (1976).

The foam cell appearance of fetal elements in stillborn infants is a very unusual occurrence. After fetal death, the placenta remains viable for a certain interval. Progressively the placental capillary system atrophies and becomes necrotic; the trophoblast atrophies, Hofbauer cells diminish, hyda-

tiform degeneration ensues; fine basophilic granular material accumulates in the trophoblastic membrane, as illustrated in our case, villous syncytial knots and cytotrophoblastic cells become more prominent and fetal stem vessels become narrowed by a fibromuscular sclerosis (Benirschke and Driscoll 1967; Fox 1978). All these changes are sufficient to invalidate any valuable histological examination of the placenta.

The foamy appearance in our case is due to regressive changes which might be tentatively explained in 2 different ways: 1) they might be an uncommon expression of degenerative transformation following fetal death; 2) they might have been caused by oedema, anoxia or local circulatory disturbances initiated before fetal death and causing changes persisting after fetal death. Recently Ginsburg and Groll reported hydrops fetalis due to infantile Gaucher's disease (1973). However, the first sibling of the case presently described did not reveal any evidence of storage disorders at autopsy.

Vacuolar degeneration is a cellular disorder usually seen in experimental conditions and as a general consequence of anoxia or toxic factors (Cameron 1952; Bell 1956; Bassi and Bernelli-Zazzera 1957; Bassi et al. 1960). In this disorder the cellular content of water is not increased and vacuoles are scattered in the cytoplasm. Our case should be more properly defined a hydropic degeneration due to increased fluid content.

It is worthwhile to note that in those storage disorders in which the ultrastructural findings consist of clear vacuoles, the vacuolar content is a finely granular medium dense material as in mannosidosis (Dickersin et al. 1980). A foamy change of stromal Hofbauer cells secondary to oedema in fetal death was described by Wilkin. However in Wilkin's account the change was restricted to the stroma of villi.

In conclusion the present case is reported not only to record an unusual histological change but also to demonstrate the necessity of a through investigation in the study of the placenta for storage disorders.

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