

OBSERVATIONS ON THE GIANT CELLS OF THE CHINCHILLA PLACENTA

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INTRODUCTION

Although a rather extensive literature exists on the giant cells of rodents, these peculiar cells still remain enigmatic in many respects. Their origin, insofar as rodents in general are concerned, has been elucidated by Mossman (1937) and, in particular, the studies of Orsini (1954) nee Ward (1948) on the origin of these cells in the hamster are classics in the field. Their function, on the other hand, has not been clearly defined, although they have generally been presumed to be phagocytic.

In their study of the development of the chinchilla placenta, Tibbitts and Hillemann (1959) made several general statements with respect to the giant cells found therein but did not treat them in detail. The present paper then seeks to expand our knowledge of these cells in the chinchilla placenta, to clarify a point with respect to their inability to divide mitotically, and to review their function(s) in light of more recent investigations on the rat and mouse.

Because of lack of suitable material to demonstrate the precise origin of the giant cells in the chinchilla, no attempt has been made to classify them according to the scheme proposed by Orsini (1954). In all probability the giant cells considered herein are secondary (placental) giant cells. This is probably

the correct appellation for the majority of the cells but the earliest ones to appear might quite possibly be primary giant cells. Only the barest evidence was revealed by this study for the existence of tertiary giant cells or endovascular cells.

MATERIAL AND METHOD

The material used had originally been collected for a study of the development and histology of the chinchilla placenta (Tibbitts and Hillemann, 1959). This consisted of placentae from 44 female chinchillas and ranged in gestation age from early egg cylinder stages to near term. Precise gestation ages could not be determined for much of the material for the reasons stated in the previous paper.

All of the material examined in the present study was fixed in Bouin's solution, embedded in paraffin and sectioned at 10 - 15 μ . Stains employed were either hematoxylin and eosin or Masson's trichrome. Measurements were made on hematoxylin and eosin stained preparations with the aid of an ocular micrometer.

OBSERVATIONS AND DISCUSSION

Tibbitts and Hillemann (1959) reported that, in their material, there was no conclusive evidence for the existence of giant cells in the

early implanatation stages of the chinchilla. Careful re-examination of these stages reaffirms the earlier statement but does not rule out the existence of giant cells. The chinchilla has a greatly reduced Träger consisting of a delicate cellular reticulum, the interstices of which are filled with extravasated maternal blood. This latter substance obscures much of the cellular elements of the Träger and renders an accurate interpretation difficult. It is quite possible that certain Träger cells were transforming into giant cells and, because of the masses of blood, escaped detection. At any rate, no cells which could unequivocally be termed giant cells or presumptive giant cells were observed peripheral to the region of the decidua occupied by the extravasated blood.

In several series of slides of material somewhat older than the foregoing but collected prior to the establishment of the chorioallantoic placenta, a few very large multinucleate cells were observed in the decidua basalis adjacent to the chorionic disc. These differed from the surrounding cells not only by virtue of their large size and multinucleate condition but, in addition, showed markedly increased cytoplasmic basophilia. These are considered to be giant cells derived from the chorionic trophoblast and probably are similar to the multinucleate masses of plasmoditrophoblast associated with the rabbit placenta (Mossman, 1937). The nuclei of these cells are small (10-15 μ in diameter) and number from 6 to 20 or more per cell.

As a general rule the nuclei of

giant cells in the chinchilla placenta are significantly smaller than those of comparable giant cells in the rat placenta. Dickson and Bulmer (1960) report mean dimensions of the largest giant cell nuclei in the rat as: length 63 μ , and breadth 18 μ . In comparison, a mean diameter of 31 μ was found for the largest giant cell nuclei in the near term chinchilla placenta.

An accurate count of these giant cells was not attempted, since the decidua basalis was quite thin and undergoing degeneration. However, it was estimated that no more than a dozen such cells were present at this time. At a comparable stage in the development of the porcupine placenta, giant cells fill a large cone-shaped zone between the chorionic disc and the decidua basalis (Perrotta, 1959). Perrotta further states that these giant cells appear vacuolated and gradually disappear during the course of placental lobulation. In the chinchilla these giant cells have a homogeneous, non-vacuolated cytoplasm and apparently disappear before or shortly after the establishment of the chorioallantois.

No evidence of true trophoblastic giant cells was seen in the stages shortly following the establishment of the chorioallantois. During this period of placental development, lateral portions of the decidua capsularis become converted into the mesoplacentalia. There is a great deal of cellular hypertrophy associated with this activity and many cells may show the large multinucleate condition frequently exhibited by trophoblastic giant cells. However, these cells intergrade with

the adjoining decidual cells and closely resemble them in all observable characteristics, other than size and number of nuclei. Furthermore, several of these large cells were observed to be in various stages of mitosis, though it has been presumed by many that trophoblastic giant cells are incapable of undergoing cell division (see below).

The next developmental stage to be considered is represented by one locus from an animal 31 days pregnant. The crown-rump length of the embryo is 38 mm. and the chorioallantoic placenta is approximately $\frac{2}{3}$ the definitive size. There is a definite layer of giant cells at the periphery of the placenta, extending from the region of the decidua basalis nearly to the sinus terminalis of the yolk sac on the fetal aspect. Small capsules of giant cells are apparent immediately adjacent to and presumably derived from the peripheral layer of giant cells. In areas where the peripheral zone is discontinuous, the capsules lie next to the junctional zone. The cells within these capsules are closely packed and typically mononucleate at this stage (Fig. 4). Infrequently they show some vacuolation of the cytoplasm or a hyaline zone (possibly representing a shrinkage artifact) just inside the cell membrane and the capsule wall appears as a relatively thick, noncellular, strongly eosinophilic membrane (Fig. 4).

These capsules of cells may extend through 10 to 15 serial sections before they eventually disappear. The capsules cannot be blood vessels filled with endovascular cells for the following reasons: (1) they can be traced from beginning to end over

a very short distance and (2) they have never been observed to contain blood cells or remnants thereof.

In addition to localization in the peripheral zone and in capsules, giant cells were also observed in the mesoplacentalia near the junction of these structures with the placenta. The giant cells here were generally mononucleate and they tended to show a more pronounced acidophilia than neighboring cells. To some extent they were associated with the maternal vascular channels, although no giant cells were ever definitely seen within the vessels (Figs. 1 and 3).

In the definitive placenta at mid-gestation, the giant cells display the following characteristics. The peripheral zone has become attenuated and in some places is discontinuous, while the cells within the capsules have greatly increased in number. Since the giant cells, at least in the hamster (Orsini, 1954) and the rat (Bridgman, 1948a, b, Dickson and Bulmer, 1960), are apparently incapable of mitotic division, the question arises as to how their increase in number occurs. Orsini assumed that, in the hamster, these cells were continuously being produced by the Träger plate and the extensions of the Träger cords. In the rat, Dickson and Bulmer postulate that the peripheral layer of giant cells can increase in area at the expense of its thickness by a redistribution of the cells, or by the addition of giant cells "from elsewhere" during placental growth.

Any one or all of these events could and probably do occur in the chinchilla placenta insofar as the giant cells of the peripheral zone or

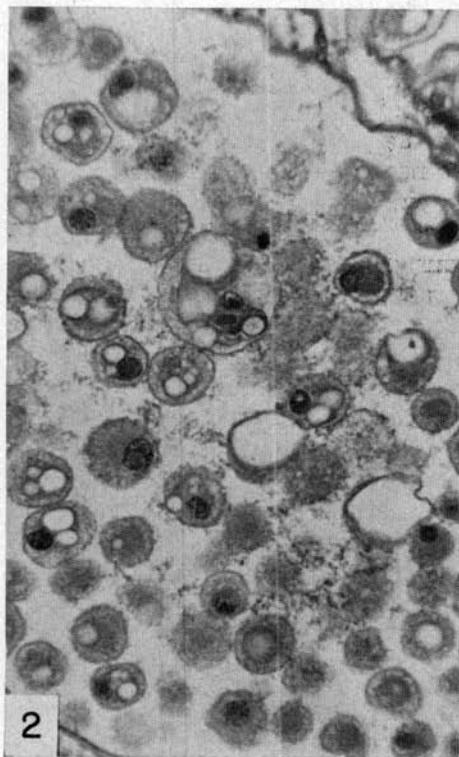


Fig. 1.—A group of giant cells in the region where the maternal blood channels leave the mesoplacentalium and enter the placental trophospongium. H. & E. X 200.

Fig. 2.—A cluster of loosely packed giant cells occurring in a capsule near the junctional zone of the chorioallantoic placenta. Notice the large vacuoles within the cytoplasm and nuclei of many of the cells. H. & E. X 200.

the mesoplacentalium are concerned. However, the question remains as to what mechanisms operate to produce the occasional multinucleate forms, or the 3 to 4 fold increase in the number of cells within a capsule. It perhaps would not be impossible for the giant cells to migrate through the wall of the capsule, but such an explanation is seemingly ruled out on the following grounds: (1) the wall of the capsule is quite thick and gives the appearance of being

rather impenetrable, (2) no cells were ever observed to have passed into or out of any of the capsules.

Secondly, it might be proposed that the giant cells arose from the wall of the capsule, but in no instance were intermediate stages seen to have originated from this source. Furthermore, the capsular wall appears to be noncellular, and it was not found to be discontinuous at any point; thus there were no portals of ingression or egression for the

enclosed cells.

The most obvious explanation would seem to be that the encapsulated giant cells, as well as those in the peripheral zone, are capable of mitotic division. Because of lack of evidence to the contrary, previous investigators have logically presumed that the giant cells are incapable of mitotic activity. However, in the chinchilla placenta we have found three indisputable cases of giant cells dividing mitotically (metaphase figures) and a number of other instances indicative of such activity. The three examples of giant cells in metaphase show the spindle fibers and chromosomes so clearly as to constitute incontro-

vertible evidence for the mitotic activity of these cells.

During midgestation the giant cells appear to be at their peak in numbers and functional activity. Nearly all of the giant cells observed at this time showed homogeneous cytoplasm and normal nuclei (Fig. 3), in contrast to the conditions found by Perrotta (1959) in the porcupine. In her study of this animal she reported that the giant cells demonstrated vacuolation and degenerative changes throughout gestation.

With respect to the function of giant cells, they have variously been described as phagocytic, producers of enzymes, or responsible for the

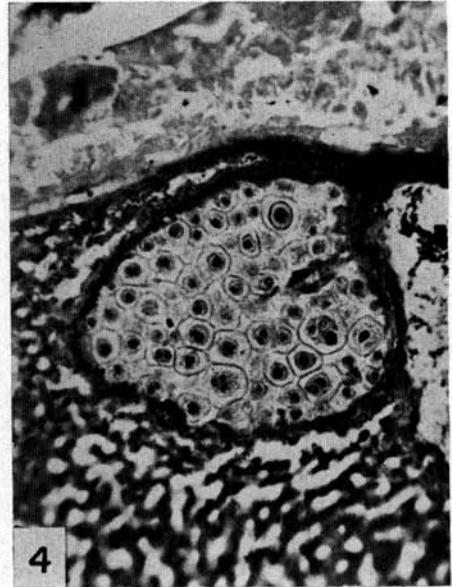


Fig. 3.—A giant cell from an area similar to that shown in Fig. 1. It is presumed that the clear peripheral zone represents a fixation-induced artifact. H. & E. X 400.

Fig. 4.—Giant cells closely packed within a strongly acidophilic capsule in the trophospongium adjacent to the junctional zone. Masson's trichrome stain. X 100.

secretion of hormones. While it is quite possible that they perform all three functions, recent workers have favored the last. Dickson and Bulmer (1960) offer the interesting suggestion that one function of the placental giant cells in the rat may be the secretion of a glyco-protein hormone into the maternal circulation. In the same year, Jollie (1960) concluded on the basis of transplantation experiments that the trophoblastic giant cells of the mouse have a rather definite life span. Once they start to regress, the reduction in the amount of luteotropic factor which they are said to produce might well result in (1) the involution of the corpora lutea, (2) the effective lowering of the progesterone level and (3) the contraction of the uterine smooth muscle which would result in parturition.

The giant cells of the chinchilla placenta never presented signs of being actively phagocytic. Intracellular inclusions which could have represented phagocytized materials were never seen. Typically the giant cell cytoplasm was similar in appearance to that of a secretory cell, although no specific substances were identified with it. In general, the present writers would ascribe primarily a secretory function to the giant cells of the chinchilla placenta, particularly the encapsulated ones at the periphery. It remains for later histochemical studies to demonstrate the nature of the secretory product(s) of these cells.

In the near term placenta many of the giant cells, particularly in the peripheral zone, exhibit extremely vacuolate cytoplasm and nuclei, and some cells are in the processes of

disintegration (Fig. 2). Presumably these are manifestations of cellular senescence which follow the reduction or loss of the cell's functional activity. If indeed the giant cells do secrete a luteotropic factor or some other substance responsible, at least in part, for the maintenance of pregnancy, then their degeneration at this time would correlate with the release of pregnancy-induced inhibition of the estrous cycle.

SUMMARY AND CONCLUSIONS

1. The first identifiable giant cells to appear in the chinchilla placenta are represented by a few very large multinucleate cells in the decidua basalis prior to the establishment of the chorioallantois. They apparently disappear before or shortly after the formation of this organ.
2. Giant cells are not seen again until the chorioallantois is well formed and approximately 2/3 the definite size. Here they appear as a discontinuous peripheral zone sheathing the placenta except on the fetal aspect. They also are seen encapsulated near the periphery and a few are found in the mesoplacentalia.
3. It was found that at least some of the giant cells are indeed capable of mitotic activity, thus explaining the increase in number of giant cells, especially the encapsulated ones, during the course of pregnancy.
4. Various functions of the giant cells are discussed. The present authors consider the giant cells

in the chinchilla to be secretory in nature, although there is no evidence at the present time as to the nature or function of the secretory product.

5. Degenerative changes such as vacuolation of the cytoplasm and nuclei are frequently seen in giant cells of the near-term placenta. These changes are presumed to be correlated with a loss of the cell's functional activity.

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