Suprasellar peri-infundibular ectopic adenohypophysis in fetal and adult brains

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Ectopic anterior pituitary cells, identified by histological, electron microscopic, and immunohistochemical methods, were consistently found in the leptomeninges of the suprasellar peri-infundibular region of fetal brains. The cell groups were not in continuity with the pars tuberalis of the adenohypophysis. Suprasellar peri-infundibular ectopic pituitary cells, which showed no neoplastic character, were found in 15 of 20 "normal" adult brains that were similarly examined. This finding sheds new light on the possible origin of intracranial ectopic pituitary adenomas.

KEY WORDS • ectopic cells • pituitary adenoma • infundibulum • pituitary cells • suprasellar tumor • fetal brain

Abundant groups of undifferentiated cells were encountered in the subarachnoid space around the pituitary stalk in fetal brains. The purpose of this study was to determine the nature of these cells, with special reference to the possible origin of certain suprasellar tumors. We discovered that these cells differentiated into ectopic pituitary cells, which were found quite frequently in adult brains.

Clinical Material and Methods

A block of the pituitary stalk was included in the routine autopsy examination of all fetal brains older than the 16th gestational week available at our institution. We also studied 20 "normal" adult brains for comparison. Blocks of specimens including the ventral hypothalamus, the pituitary stalk, and the dorsal part of the pituitary were embedded in paraffin, cut serially, and examined histologically with hematoxylin and eosin (H & E) and Pearse staining techniques. Eighteen pituitary stalks were cut coronally, one horizontally, and one sagittally.

Electron microscopic study was undertaken on eight randomly selected fetuses ranging in age from 31 to 41 gestational weeks. Pituitary stalks and glands were excised from unfixed brains, fixed in glutaraldehyde, and embedded in Araldite. For immunohistochemical examination, pituitary stalks from 10 cases (four fetuses, two infants, and four adults) were tested in paraffin sections with peroxidase-antiperoxidase (PAP) reactions to somatotropic hormone.

Results

In fetal brains, thick cell cuffs intimately surrounded the infundibulum and the pituitary stalk (pars tuberalis or pars infundibularis of the adenohypophysis) at 16 to 18 weeks of gestation. Rosette structures were also encountered in the cell cuffs. The cells were poorly differentiated, and small amounts of cytoplasm were recognizable after 18 weeks of gestational age. The nuclei were round and consistently dark. Islands of aberrant cells, similar to those of the pars tuberalis, were found in all routinely examined fetal brains; they were located within the leptomeninges surrounding the pituitary stalk and the infundibulum, not in continuity with the pars tuberalis (Fig. 1). Rosette structures and non-birefringent mineralized deposits were encountered in the aberrant cell aggregates. The deposits appeared identical to those found in the pituitary after 20 weeks of gestation. From the 30th gestational week on, the peri-infundibular ectopic cells were similar to those of the adenohypophysis examined in routine histological preparations.

In adult brains, suprasellar ectopic pituitary gland cells were identified in 15 (75%) of the 20 cases examined. They were always found in the leptomeninges of the peri-infundibular region (Fig. 2). Again, there was no connection between ectopia and the pars tuberalis. The ectopic cells included acidophil, basophil, and chromophobe cells.

On electron microscopy, two types of ectopic cell could be distinguished in the immature and mature...
neonatal brains: a dark and a clear type (Fig. 3). Both types were randomly distributed in the ectopic islands, including the rosettes. The protoplasm of the dark cells was dense while the clear cells stained less intensely. Both types of cells contained round electron-dense secretory granules, which were slightly smaller and more irregularly formed in the clear cells. The irregular surface of the cells facing the lumina of the rosettes had no recognizable cilia. Several desmosomes were recognized. The nuclear structure of both types was similar except for the denser appearance of the dark cells.

In all cases examined, including fetuses, reaction to somatotropic hormone was positive in many ectopic peri-infundibular cells in immunohistochemical studies (Fig. 4). In the youngest fetus examined, which was 18 weeks of gestational age, the reaction was only slightly positive in a few ectopic cells as well as in the anterior pituitary cells.

Discussion

This study shows the frequent existence of suprasellar peri-infundibular ectopic pituitary tissue in normal brains. Electron microscopic and immunohistochemical examination confirmed the identity of the ectopic cells as similar to those of the anterior pituitary. The ultrastructural appearance of the dark and clear cells corresponded to somatotropic and gonadotropic cells, respectively. The undifferentiated appearance of the peri-infundibular cells in the fetal brains was consistent with differentiating pituitary cells. On immunohistochemical examination, the ectopic peri-infundibular cells showed functional differentiation around the 18th gestational week. Somatotropic hormone can be used as an immunohistochemical marker for the ectopic pituitary cells.

The adenohypophysis develops from Rathke’s pouch, and is seen as early as the 6.5-mm embryonal stage. It loses its attachment to the pharyngeal roof by rupture of its stalk. Ectopia of the adenohypophysis in the infrasellar region, known as pharyngeal pituitary, occurs by partial persistence of the pouch in the wall of the buccal cavity, craniohypophyseal canal, or sphenoid sinus during the 12- to 20-mm stage. Aberrant suprasellar adenohypophysis may originate later when the pars tuberalis develops from the pars anterior of the pituitary at the 41- to 55-mm stage. Because the adenohypophysis originates extracranially and only later becomes attached to the neurohypophysis, the pituitary cells may easily be displaced in the leptomeninges of the peri-infundibular region.

The question is repeatedly raised whether ectopic tumors arise from normal aberrant tissues. In this respect, the occurrence of pharyngeal pituitary adenomas, described probably for the first time by Erdheim, might also be considered. Only one case of suprasellar ectopic pituitary adenoma has been reported in the literature; the authors observed a chromophobe adenoma inferior to the third ventricle with a normal adenohypophysis. They suggested the possibility of normal pituitary tissue occurring in a suprasellar location. Their hypothesis is corroborated by our observations. In our series, we found no evidence of neoplastic alteration in the ectopic pituitary tissue.

The pharyngeal location of pituitary cells is a constant finding. We have found that ectopic pituitary cells are almost always present in the leptomeninges of the suprasellar region. They may be possible bases for the occurrence of a suprasellar ectopic adenoma. The number of ectopic cells is most likely not sufficient to produce effective hormonal compensation for an ablated pituitary gland.

Amyloid deposits are occasionally noted in adult prolactinomas. Small amounts of mineralized deposits...
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FIG. 3. Electron micrographs showing the ultrastructure of the ectopic cells in a specimen from a fetus of 31 weeks gestational age. Left: Rosette structure with dark and clear ectopic cells. Collagen fibers of the leptomeninges are seen at the bottom of the picture. × 2470. Right: Section showing dark and clear cells, both of which contain secretory granules. × 3700.

FIG. 4. Immunohistochemical preparation of a specimen from a fetus in the 20th week of gestation. Reaction to somatotropin hormone is positive in many of the intrameningeal ectopic cells (arrows). A mineralized deposit (M) is also seen. PAP, × 388.

were recognizable in the pituitary gland of normal fetuses as early as after the 20th gestational week. These deposits were also encountered in association with the ectopic cells in the fetal brains examined here (Fig. 4).

Addendum

After submission of this manuscript, a report was published on the suprasellar ectopic pituitary gland in two children with craniopharyngioma (Decker RE: The ectopic pituitary gland in cases of craniopharyngioma. Report of two cases, J Neurosurg 62:291–292, 1985). In these cases, the ectopia was a macroscopically recognizable mass, either a dysmorphic and dislocated part of the ordinary pituitary gland or isolated pituitary tissue. Our present report does not concern an ectopic mass but pituitary cell groups which are almost always observed in normal individuals at the microscopic level.

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