Modern Approaches to Classification of Pituitary Tumors in Human Subjects and Animals

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Normal Pituitary

Development and Anatomy. The adenohypophysis originates in a diverticulum of stomodeal ectoderm called Rathke's pouch. A ventral evagination of diencephalon-saccus infundibuli contacts Rathke's pouch and gives rise to the neurohypophysis. The adenohypophysis has an anterior lobe, pars intermedia, and pars tuberalis. The anterior lobe (pars distalis, pars glandularis) is composed mainly of hormone-producing cells. The chronologic appearance of different cell types during intrauterine development has been established by immunocytochemistry (Setalo and Nakane 1976; Chatelain et al. 1979; Osamura and Watanabe 1985). In man and rodents the first detected are adrenocorticotropin (ACTH) immunoreactive cells and growth hormone (GH) immunoreactive cells (5–18 weeks and 16 days of gestation, respectively) followed by cells containing glycoprotein hormones such as thyrotropin (TSH), follicle-stimulating hormone (FSH), and luteinizing hormone (LH; 12 weeks and 17–18 days, respectively). The last to appear are prolactin (PRL) immunoreactive cells; their number increases markedly at term in man and postnatally in the rat.

The intermediate lobe in humans is rudimental, being represented by a few follicles. Their cavities are the vestigial lumen of Rathke's pouch. In rodents the intermediate lobe is well developed and is separated from the anterior lobe by a cleft, the residual cavity of Rathke's pouch. It is formed by cells immunoreactive for ACTH and other proopiomelanocortin (POMC) derived peptides that are detected in the rat during gestation at day 17.

The pars tuberalis is formed by clusters of glycoprotein hormone-containing cells. In the human pituitary, islets of squamous cells are present as well. The neurohypophysis consists of the median eminence, hypophysial stalk and posterior lobe. The hypophysial stalk is composed mainly of axons and portal vessels. The axons originate in magnocellular neurons of supraoptic and paraventricular nuclei of the hypothalamus that transport vasopressin and oxytocin to the posterior lobe. The portal vessels transport the hypothalamic releasing and inhibiting hormones to the adenohypophysis.

Morphology: Adenohypophysis. On horizontal cross-section the anterior lobe of human adenohypophysis is divided in a central mucoid wedge and two lateral wings, delineated by a thin fibrous trabecula. The somatotrophs are located mainly in the lateral wings, and the corticotrophs and thyrotrophs in the mucoid wedge. The lactotrophs and gonadotrophs are scattered throughout the gland. The hormone-containing cells are dispersed in acini surrounded by a basement membrane (Kovacs and Horvath 1986).

In rodents the glandular cells have no clearcut preference for a certain area of anterior lobe (Poole and Kornegay 1982), and no acinar structures are found. The groups of cells are separated by a rich fibrovascular network. The different cell types of the adenohypophysis are characterized based on hormone content and ultrastructural features (Fig. 55; Kurosumi 1968; Horvath and Kovacs 1988).

Somatotrophs (GH cells) are acidophilic and are the predominant cell type (40%–50%; Fig. 56). Electron microscopy reveals densely granulated cells with secretory granules ranging in diameter between 300 and 400 nm in rat and mouse and up to 500 nm in man. A minority of cells possess
small secretory granules of 150 nm. GH secretion is under the hypothalamic control. Growth hormone releasing hormone (GRH) via portal vessels stimulates GH release, while somatostatin (SRIF) has the opposite effect.

Lactotrophs (PRL cells, mammotrophs) in humans vary in number according to age, sex, parity, and hormonal status. In rodents the lactotrophs are more numerous in females (45%) than in males (24%; Fig. 57; Sasaki and Iwama 1988). During pregnancy in women a gradual, diffuse lactotroph hyperplasia occurs that is easily identified by light microscopy (Stefaneanu et al. 1992a) while in rats the diffuse increase in number of lactotrophs is mild. In most lactotrophs PRL immunostaining shows a paranuclear globular pattern corresponding to the Golgi apparatus rich in forming secretory granules. In humans the secretory granules are rather small (about 150–200 nm) while in rodents they are markedly pleomorphic, measuring up to 800 nm. The extrusion of secretory granules into the intercellular space, the hallmark of human lactotrophs, occurs in rat and mouse, not only in this cell type but in somatotrophs as well. Under sustained GRH stimulation the frequency of extruded granules increases in somatotrophs (Stefaneanu et al. 1993). In humans rare densely granulated lactotrophs with secretory granules of 250–450 nm are identified. In rodents a second type of lactotroph with small secretory granules (200 nm) is present, especially in males.

PRL secretion is inhibited by dopamine produced by the hypothalamus. As PRL-releasing factors, thyrotropin-releasing hormone (TRH), vasoactive intestinal polypeptide (VIP), angiotensin II, and neurotensin are proposed. Among peripheral hormones estrogen is a powerful stimulator of PRL production.

Mammosomatotrophs, bihormonal cells producing GH and PRL, have been identified in a small percentage by different techniques, such as reverse hemolytic plaque assay, immunocytochemistry at the light and electron microscopic level and in situ hybridization combined with immunocytochemistry (Frawley and Boockfor 1991).

Corticotrophs (ACTH cells) are basophilic cells, immunoreactive for POMC derived peptides, such as ACTH, melanocyte-stimulating hormones.

Fig. 55. Normal rat anterior lobe depicting somatotroph (gh), a thyrotroph (th), and a lactotroph (lt) with an extruded secretory granule (arrow). TEM, x4500