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Immunocytochemical evidence for the ability of the human pharyngeal hypophysis to respond to change in endocrine feedback *

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Summary. Two pharyngeal hypophyses from patients with endocrine disorder were examined light microscopically and immunocytochemically. The pharyngeal hypophysis from a patient with primary hypothyroidism was hypertrophic, with TSH cell hyperplasia; while that from a patient treated with metoclopramide, a dopamine-receptor-blocking drug, showed PRL cell hyperplasia. These findings strongly suggest that under certain circumstances the pharyngeal hypophysis is able to respond with specific changes to variations in the endocrine feedback.

Key words: Pharyngeal pituitary – Immunocytochemistry – Hypertrophy – Hyperplasia

Introduction

The human pharyngeal hypophysis is a constant structure present in the periosteum of the nasopharynx (Erdheim 1904); composed of cells arranged in cords, interspersed with strands of connective tissue and small blood vessels (Romeis 1940). Immunocytochemical studies of the human pharyngeal hypophysis have shown the presence of adrenocorticotropic hormone (ACTH) (Hachmeister 1967) and growth hormone (GH) (McPhie and Beck 1968) cells. In a recent study, we confirmed the presence of ACTH and GH immunoreactive cells in pharyngeal hypophyses from patients with no evidence of endocrine disorder (Ciocca et al. 1985). This study has also shown the presence of follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL), thyroid-stimulating hormone (TSH), and lipotropin (LPH) immunoreactive cells in the pharyngeal hypophysis. However, there are no detailed immunocytochemical studies on the morphological

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response of these cell types to change in endocrine feedback. The relatively few studies on the ability of the pharyngeal hypophysis to play a compensatory role in pituitary function are controversial (Melchionna and Moore 1938; Van Buren and Bergenstal 1960; McGrath 1969; McPhie and Beck 1973; McGrath 1978). The present report describes the pharyngeal hypophysis from a patient with primary hypothyroidism associated with a sellar pituitary adenoma; and from a patient with bronchopneumonia and vomiting, who had also received metoclopramide, a dopamine-receptor-blocking drug.

Report of Two Cases

Case 1. A 15-year old girl was admitted to the hospital in June 1983 in hypothyroid coma, dying 24 h after admission. She had congenital hypothyroidism recognized during the second month of life, treated with levothyroxine sodium until two months before admission, when she suddenly discontinued the therapy. The autopsy findings revealed normal physical and sexual development, dehydration, intestinal obstruction (paralytic ileus), agenesis of the thyroid gland, and a pituitary adenoma of 2 cm in diameter with severe compression of the residual parenchyma of the anterior lobe.

Case 2. An 84-year old man was admitted to the hospital in June 1983 for bilateral bronchopneumonia, vomiting and malnutrition, dying two days after admission. He had been treated with penicillin, vitamins, dextrose solution, and metoclopramide (30 mg/day i.v.). He had been receiving metoclopramide, for an undetermined period, before admission. Remarkable autopsy findings were bronchopneumonia, arteriosclerosis and benign prostatic hypertrophy.

Blood hormone levels were not available for correlation with histological findings.

Materials and methods

The pharyngeal hypophyses were dissected out within a period of 6 h after death, following the method of Melchionna and Moore (1938). The glands were fixed in 10% formalin, and under a dissecting microscope the area containing the pharyngeal hypophysis was trimmed as much as possible. After dehydration in a graded ethanol series, the glands were cleared in xylene and embedded in paraffin. The material was oriented to obtain longitudinal sections of the gland. Deparaffinized serial sections, 4–6 μm in thickness, were stained with haematoxylin-eosin (H& E), Masson's trichrome, or immunostained with the indirect peroxidase technique using the peroxidase-antiperoxidase method (PAP) and the avidin-biotin-peroxidase complex (ABC) system as described previously (Childs (Moriarty) and Unabia 1982). The antisera were used at the following dilutions: 1:7,500 (anti-pACTH$^{1-39}$); 1:10,000 (anti-hPRL, anti-hFSHβ, anti-hLHβ, anti-hβLPH); and 1:100,000 (anti-hGH, anti-hTSHβ). The antibodies were applied on the etched slides and incubated for 72 h in humidity chambers, at 4° C. They were provided and their specificity assessed by the Pituitary Hormone Distribution Program of the National Institute of Arthritis, Diabetes, and Digestive and Kidney diseases (NIADDK), Baltimore, Maryland. Controls for the immunocytochemical reaction were substitution of the primary antibody for 3% normal rabbit serum or normal goat serum, and dissapearance of immunostaining after specific immunoabsorption with the corresponding purified hormone. The quantitative analysis of the immunoreactive cell types was done by two observers counting those cells that contained nuclei as previously described (Asa et al. 1982).

Microscopic Findings. The pharyngeal hypophysis from the patient with hypothyroidism (Fig. 1) was larger (double size) than those obtained from patients without endocrine disorders (Ciocca et al.), or from the patient treated with metoclopramide (Fig. 2). The pharyngeal hypophysis of the hypothyroid patient was composed of cords or clusters of cells with relatively abundant cytoplasm and round-oval nuclei with prominent nucleoli (Fig. 1). In this case, immunocyto-

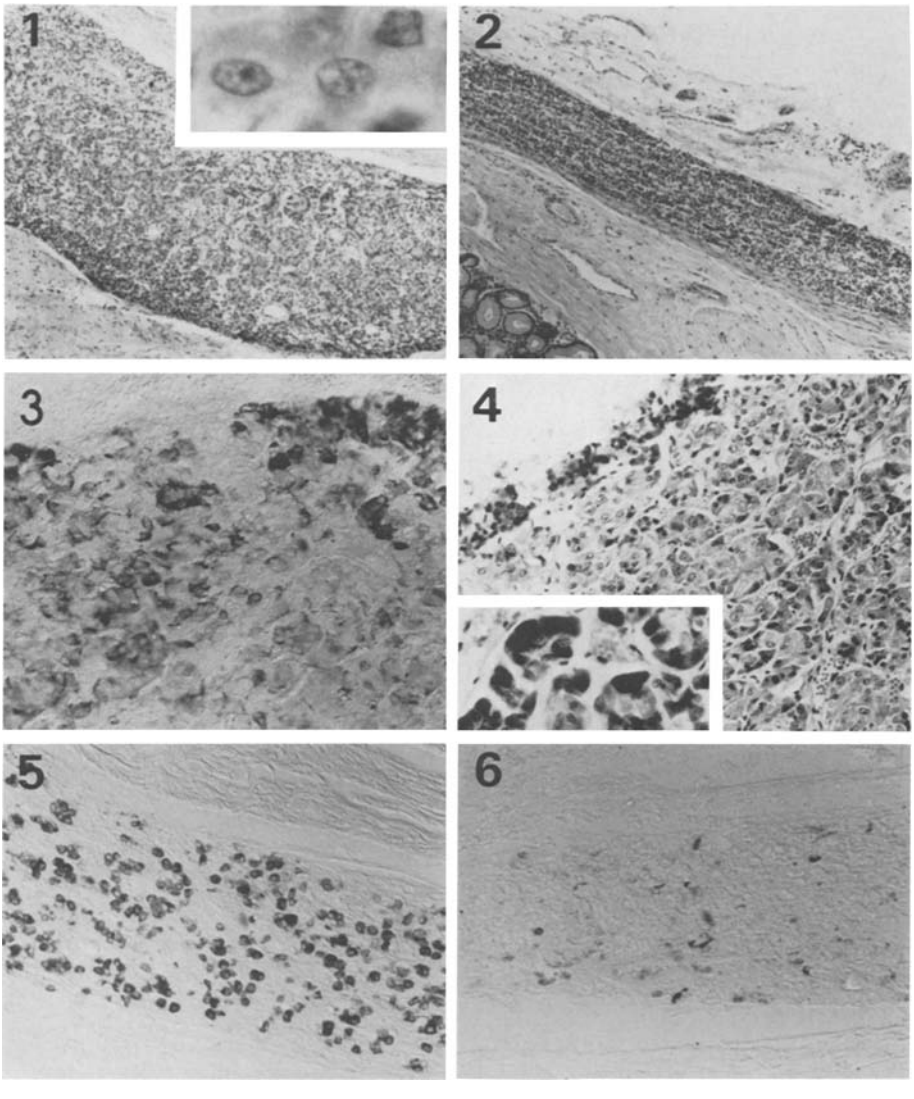

Fig. 1. Pharyngeal hypophysis from the patient with primary hypothyroidism. Note the enlargement of the gland (compare with Fig. 2) (H & E stain, × 55). *Inset:* under higher magnification, the characteristics of the cells can be seen. (H & E stain, × 500)

Fig. 2. Pharyngeal hypophysis from the patient treated with metoclopramide. (H & E stain, × 55)

Fig. 3. Pharyngeal hypophysis from the patient with hypothyroidism. Note the hyperplasia of TSH cells. (ABC immunostaining, × 120).

Fig. 4. Sellar adenoma of the hypothyroid patient. Note the compression of the residual parenchyma of the anterior lobe (*left upper corner*). (H & E stain, × 120). *Inset:* an area of the sellar adenoma showing numerous LPH cells. (ABC immunostaining with haematoxylin counterstain, × 130)

Fig. 5. Pharyngeal hypophysis from the patient treated with metoclopramide. PRL cells predominate in the gland (compare with Fig. 6). (ABC immunostaining, × 120)

Fig. 6. Pharyngeal hypophysis from the patient treated with metoclopramide. In this case, a few FSH cells are interspersed among the unstained cells (ABC immunostaining, × 100)

Table 1. Comparative Percentages of Immunoreactive Cells

Immunoreactive Cell	Percentage		
	Pharyngeal hypophysis Case # 1	Pharyngeal hypophysis Case #2	Sellar adenoma Case # 1
PRL	17.0±2.8	57.0±0.2	25.4±0.1
GH	5.0±0.4	24.8±1.0	3.7±1.9
LH	1.8±1.1	4.5±0.1	–
FSH	27.4±7.8	9.9±0.4	1.8±0.9
TSH	45.5±5.6	1.6±0.4	5.4±2.1
LPH	7.9±0.2	4.0±1.3	48.5±5.9
ACTH	3.4±1.5	0.7±0.1	20.4±2.5

chemistry revealed that the pharyngeal pituitary population was composed predominantly of TSH cells, displaying different immunostaining intensity (Fig. 3). These cells were distributed randomly throughout the pharyngeal hypophysis. The other cell types studied were also identified but with lower incidence. The quantitative analysis indicated TSH cell hyperplasia (Table 1).

The sellar pituitary gland of the patient with hypothyroidism showed a mixed adenoma composed predominantly by LPH (Fig. 4), ACTH, and PRL immunoreactive cells. Most of the time these cell types were arranged in clusters in areas of the adenoma. The strongest immunostaining was seen in the LPH cells, followed by the PRL cells. The ACTH cells showed relatively weak immunostaining. There were also GH, TSH, and FSH cells scattered in the adenoma, but the frequency of occurrence of these cells was low (Table 1).

The pharyngeal hypophysis from the patient treated with metoclopramide had normal dimensions (Fig. 2) but it was composed predominantly by PRL immunoreactive cells (Fig. 5). These cells were randomly distributed throughout the gland and showed variable immunostaining intensity. This pharyngeal hypophysis also showed numerous GH immunoreactive cells while the other cell types were scarce (Fig. 6). The quantiative analysis revealed PRL cell hyperplasia (Table 1).

Discussion

The histological and immunocytochemical features of the two pharyngeal hypophyses examined suggest that this gland has the capacity to respond with specific changes to endocrine abnormalities. This was clearly seen in the patient with hypothyroidism, where the gland appeared hypertrophic, with TSH cell hyperplasia. In the normal human pharyngeal hypophyses studied by immunocytochemistry (Ciocca et al. 1985), the percentage of TSH cells was always under 20%; while in the present case it was 45%. The hyperplasia of these cells is explained by the absence of the thyroid gland and of replacement therapy at the end of life. It is also possible that the hypertrophy and hyperplasia of the pharyngeal hypophysis was enhanced by the presence of the sellar pituitary adenoma. In this case, the sellar hypophysis was unable to respond to the change in the endocrine feedback since it was occupied by the adenoma.

On the other hand, the pharyngeal pituitary gland from the patient treated with metoclopramide showed PRL cell hyperplasia. Unfortunately, the sellar hypophysis of this patient was not available to study the number

of PRL cells. However, the maximun percentage of PRL immunoreactive cells in the human normal adenohypophysis (Asa et al. 1982) and in the human normal pharyngeal hypophysis (Ciocca et al. 1985) is about 30%; while in the present case it reached 57%. The hyperplasia of PRL cells may be attributable to the dopamine-receptor-blocking drug since it stimulates PRL secretion in man (Aono et al. 1978). Nevertheless, since this patient was highly stress the possibility that the stress itself was also affecting the number of PRL cells cannot be ruled out.

In both cases the cellular appearance of the pharyngeal pituitary gland was affected, but the study does not clarify whether such modifications occurred via the hypothalamic-adenohypophyseal system or without the involvement of hypothalamic connection. Previous studies have pointed out that the pharyngeal hypophysis is a part of the hypothalamic-adenohypophyseal system (Hachmeister 1967; McGrath 1972).

The possibility that the pharyngeal hypophysis might play a role in endocrinologically-disturbed patients is controversial. Before the advent of immunocytochemical methods, the histological findings in pharyngeal hypophyses from hypophysectomized patients showed no evidence of hypertrophy and/or hyperplasia of the gland (Van Buren and Bergenstal 1960). Previous studies also failed to find significant changes in pharyngeal pituitary glands from patients with pregnancy or with tumors of the sellar hypophysis (Melchionna and Moore 1938). However, there are morphological studies showing evidence of pharyngeal pituitary modifications in patients with hypophysectomy or anencephaly (McGrath 1969 and 1978). Using immunocytochemistry, ACTH cells were found in pharyngeal hypophyses from patients without endocrine disorders; and in a patient with a Cushing's syndrome, the pharyngeal pituitary gland revealed Crooke's cells (Hachmeister 1968). In contrast, there was no evidence of hyperplasia of GH immunoreactive cells in the pharyngeal hypophyses from endocrinologically-disturbed patients (McPhie and Beck 1973). The two cases reported in the present study strongly suggest that the pharyngeal hypophysis has the ability to undergo specific changes in patients with endocrine imbalance. However, it is possible that the pharyngeal hypophysis can respond in certain patients and not in others. Therefore, a large number of pharyngeal hypophyses from patients with endocrine disorders should be studied before more conclusions are drawn on this subject.

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