PITUITARY CYST OF RATHKE'S CLEFT ORIGIN
WITH HYPOPITUITARISM

VEERASAMY S. NAIKEN, M.B., Ch.B., MILTON TELLEM, M.D.,
AND DAVID R. MERANZE, M.D.

Department of Pathology, Albert Einstein Medical Center, Southern Division,
Philadelphia, Pennsylvania

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Pituitary adenoma most frequently is the cause of hypopituitarism occurring in adult life. However, a pituitary cyst, with certain distinctive histologic features pointing to an origin from Rathke's cleft, may be the pathologic cause. The rarity of this condition is evidenced by the paucity of published reports. Some of the patients, in the reported cases, had signs of hypopituitarism, others had a predominance of effects of pressure on nearby structures.

The incidental finding, post mortem, of such a cyst, in an elderly man who clinically had presented signs of myocardial infarction and hypopituitarism, warranted this report. It deals with the embryologic and morphologic aspects of the cyst together with the clinical and laboratory findings.

CLINICAL ABSTRACT

A 72-year-old negro male was first hospitalized at the Southern Division of Albert Einstein Medical Center, Philadelphia, on Sept. 11, 1957 with precordial pain and dyspnea of 11 years' duration, and vague abdominal pain of 8 years' duration, associated with slight nausea and vomiting. Food and alkali relieved the gastrointestinal symptoms. A recent loss of ~0 pounds in weight had occurred over a 6 months' period. He had one son, aged 46, well in all respects. The patient had stopped consumption of alcohol some 10 years previously.

Examination. Systemic review revealed dyspnea, "two-pillow" orthopnea and frequent paroxysmal nocturnal dyspnea. He preferred hot weather. There was loss of pubic hair in the past 4 years. He wore glasses, but did not suffer from headaches or visual disturbances.

The main findings, on physical examination, were the total absence of beard, pubic and axillary hair; female configuration of the trunk; a pale, smooth and glassy-looking skin; a dry scaling over the dorsum of the right hand; and a high-pitched voice. The testes appeared atrophic. The eyegrounds and visual fields were normal. He was 5 feet 8 inches in height and weighed 165 pounds.

Hemogram, blood electrolytes and urinalyses were within normal limits. The upper and lower gastrointestinal series were negative except for narrowing of the pyloric antrum. Gastric analysis revealed normal acidity. Electrocardiography showed right bundle-branch block with ischemia of the anterior wall of the left ventricle. Radiography of the skull revealed destruction of the dorsum sellae and posterior clinoids, secondary to an intrasellar space-taking mass. Specklike calcifications were present in the region of the sella (Fig. 1). The cerebrospinal fluid showed no abnormalities. Endocrinological studies on urine and blood done during both admissions are listed in Tables 1, 2 and 3. A 24-hour urine examined for gonadotropin in September 1957 was 5 rat units (our normal, 10 to 24 rat units/day). While in the hospital, the patient was treated for a presumed gastric ulcer, and given, in addition, Acthar gel 40 units, twice daily.

Course. He was re-admitted on Sept. 9, 1959 with an acute exacerbation of the precordial pain with definite radiation to the right arm. Electrocardiography confirmed the clinical suspicion of acute myocardial infarction. He had no symptoms referable to the pituitary lesion. The blood count and serum electrolytes were within normal limits. The physical signs of pituitary insufficiency and the cranial findings were unchanged. Despite vigorous treatment for congestive heart failure, his condition deteriorated and he expired 17 days after hospitalization. The clinical diagnoses were acute myocardial infarction and hypopituitarism secondary to a pituitary adenoma.

Pathological Examination. Autopsy was performed 3 hours after death. Gross findings. The external features were those seen clinically.

Attached to the brain in the region of the pituitary stalk was the wall of a collapsed cyst, measuring 1.5 cm. in diameter, the fluid content of which was lost during removal of the brain. The mammillary bodies and adjacent structures at the base of the brain were distorted and displaced in an upward and posterior direction, and more towards the left. No tumor was seen in the pituitary fossa. The pituitary gland was not found, but the sella contained loose fibrous tissue. There were erosion and destruction of the posterior clinoids and dorsum sellae.

The thyroid gland weighed 10 gm. and was small, firm, gray-yellow and fleshy. Both adrenals weighed together 11.5 gm. and had thinned cortices. The testes had a combined weight of 21 gm. and were firm. The rest of the autopsy disclosed the following: extensive healing myocardial infarctions of the anterior wall of the left ventricle and interventricular septum, associated with marked atheromatous narrowing of the descending branch of the left coronary artery; bilateral pleural effusion; and a finely nodular cirrhosis of the liver.

Microscopic findings. Sections of the pituitary cyst showed the walls to be thrown into papillary folds and lined, for the most part, by tall columnar ciliated epithelium with interspersed goblet cells. A layer of small conical basal cells was present between the columnar cells and the well-formed basement membrane. The
TABLE 1

Endocrine studies

<table>
<thead>
<tr>
<th>Urinary 17-OH Corticoids</th>
<th>Urinary 17-Ketosteroids</th>
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</thead>
<tbody>
<tr>
<td>(24-Hour Urine Output)</td>
<td>(24-Hour Urine Output)</td>
</tr>
<tr>
<td>9/23/57 Before ACTH test</td>
<td>0.22 mg.</td>
</tr>
<tr>
<td>After 40 units ACTH</td>
<td>0.39 mg.</td>
</tr>
<tr>
<td>10/9/57</td>
<td>0.39 mg.</td>
</tr>
<tr>
<td>10/11/57</td>
<td>0.39 mg.</td>
</tr>
<tr>
<td>10/24/57</td>
<td>0.66 mg.</td>
</tr>
<tr>
<td>(2 years later)</td>
<td></td>
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<tr>
<td>Normal values (total)</td>
<td>2.9–14 mg./day</td>
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</tbody>
</table>

cytoplasm of the ciliated columnar cells was vacuolated, and the nuclei were situated mostly in the center of the cells. Goblet cells occurred in groups of two or more, a picture suggesting intestinal epithelium or mucus-secreting salivary gland. The contents of the goblet cells gave positive reactions with periodic acid Schiff and mucicarmine stains. The columnar ciliated cells gave way, in many areas, to many-layered cells, also lined luminally by cilia. In still other but rare zones, the lining consisted of a single layer of cuboidal cells devoid of cilia (Figs. 2 and 3).

The stroma immediately adjacent to the lining epithelium was loose and edematous and showed few fibroblasts. Further away, the stroma was collagenous, and in these areas there were surviving foci of anterior pituitary cells with adjacent pars nervosa. These anterior pituitary cells were mainly amphophilic, showing minimal granularity by the periodic acid Schiff stain (Fig. 4). There were multiple foci of calcification in the stroma and in the walls of the large arteries. There was no evidence of neoplasm. Sections of brain, particularly those from the hypothalamus, disclosed no abnormalities.

The testes showed complete testicular atrophy with absence of Leydig cells (Fig. 5). The thyroid was replaced extensively by lymphoid tissue with definite formation of follicles and germinal centers. Scattered islands of small thyroid follicles with flattened epithelium containing pale to pink-staining colloid were present (Fig. 6). The adrenal cortices were markedly thinned (Fig. 7). The gross impressions of healing and healed myocardial infarctions and inactive nutritional-type of cirrhosis of the liver were confirmed.

Our final diagnoses were: Pituitary cyst; old and healing myocardial infarctions with advanced occlusive coronary arteriosclerosis; bilateral pleural effusion; Laennec’s cirrhosis of liver; atrophy of testes; moderate atrophy of thyroid; and clinical hypopituitarism.

DISCUSSION

An unusual feature in this cyst is the presence of columnar ciliated epithelium in its lining. A better understanding of the origin of such a cyst probably can be obtained after the development of the hypophysis cerebri has been reviewed.

Embryologically, the hypophysis arises from two anlage. The pars buccalis develops from an evagination of the buccal mucosa known as Rathke’s pouch. This begins in the 3 mm. human embryo and grows upward toward the ventral surface of the neural tube. Various claims as to the ectodermal or entodermal origin of the hy-