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Double Tumors of Anterior and Posterior Pituitary Gland

T. Tomita, M. Kuziez, and I. Watanabe

Department of Pathology, University of Kansas Medical Center, Kansas City, KS 66103, USA

Summary. Double tumors were found in the anterior and posterior lobes of pituitary gland at autopsy in a patient who presented with progressive deterioration of mental status. The chromophobe adenoma of anterior lobe consisted of a mixture of non-immunoreactive hormone containing cells and a few prolactin (PRL) and growth hormone (GH) cells in the mid portion whereas the periphery of the tumor contained immunoreactive cells for PRL, GH, thyroid-stimulating hormone (TSH), luteinizing hormone (LH), and follicle-stimulating hormone (FSH). A microscopic focus of granular cell myoblastoma (GCM) was found in the posterior lobe. Differentiation of tumor cells into anterior pituitary cells and GCM is discussed.

Key words: Pituitary adenoma – Granular cell myoblastoma – Immunocytochemistry

So-called chromophobe adenomas represent about 50% of all pituitary adenomas. They are usually nonfunctioning or non-secretory, however, almost always contain secretory granules (McCormick et al. 1971; Kovacs et al. 1976). Furthermore, serum PRL levels were elevated in at least one-third of the patients with pituitary adenomas (Tolis et al. 1974; Ezrin et al. 1978). The immunoperoxidase staining for PRL was at least focally positive for the chromophobe adenomas (Kovacs et al. 1976; Tolis et al. 1974).

GCM is relatively uncommon and the head and neck are the most common locations (Kanabe et al. 1978). Symptomatic pituitary GCM is extremely rare, although incidental findings of small GCM are relatively common, estimated as about 6% of pituitary glands examined by autopsy (Doron et al. 1965). These GCM lesions were not seen in the pituitary glands of persons less than 20 years of age (Satyamurti et al. 1972). In this paper double tumors of chromophobe adenoma and GCM are presented. The combination of these double tumors had not been reported to our knowledge.

Offprint requests to: T. Tomita, MD (address see above)

Case Report

A 66-year-old white man was admitted with a 3-week history of deteriorating mental status, manifested by progressive confusion and bizarre behavior. The work-up including skull X-ray, CT scan, cerebrospinal fluid analysis, and urine screen for heavy metals did not reveal an etiology. Serial EEGs were consistent with diffuse cerebral dysfunction. Subsequently, he had several episodes of severe pneumonia, urinary tract infection and sepsis, which were treated with numerous antibiotics. Seven months after admission, he died of bronchopneumonia. At autopsy the brain weighed 1,320 g, and there were no abnormalities by gross and microscopic examination.

The pituitary gland was grossly normal, measuring 1.0 × 0.55 cm. The entire gland was fixed in phosphate buffered 10% formaldehyde.

Material and Methods

One half of the bisected pituitary gland was submitted for routine histological examination, including H&E, PAS with and without diastase digestion, Orange G-PAS, Masson's trichrome, and Bodian's staining. For immunoperoxidase method, sections 5 μm in thickness were deparaffinized, refixed in Bouin's for 24 h and processed for indirect peroxidase conjugate method (Nakane 1976; Taylor 1978) for detecting the presence of anterior pituitary hormones using the following monospecific antisera: rabbit human pituitary PRL antiserum, rabbit human GH antiserum, rabbit human pituitary TSH beta antiserum, rabbit human LH beta antiserum, and rabbit human FSH beta antiserum (all of the antisera were supplied by the National Pituitary Agency, NIAMDD, Baltimore). Goat anti-rabbit gamma globulin was purchased from Cappel Laboratory, Cochranville, PA, USA and was conjugated with horseradish peroxidase (Sigma Chemical, St. Louis, MI, USA) according to the method of Avrameas et al. (1971). A small piece of tissue containing the GCM was dissected from the other one-half of the gland, post-fixed in osmium tetroxide and embedded in Epon 812 after dehydration in graded ethanol.

Results

Histologic Findings

The anterior lobe contained an adenoma, measuring 0.3 × 0.25 cm in largest dimension. The tumor was

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located in the inferior portion of anterior lobe, in close contact with fibrous capsule of the gland (Fig. 1). The tumor was not capsulated and gradually transformed into the surrounding normal anterior gland (Fig. 2A). The tumor consisted of round to polygonal cells arranged in a trabecular pattern of up to a few cell layers (Fig. 2 A). The tumor cells contained prominent nucleoli with poor chromatin and scanty cytoplasm with generally amphophilic staining. No definite secretory granules were observed by Orange G-PAS staining.

Located in the inferior portion of posterior gland was a small GCM, measuring 0.25 × 0.10 cm in greatest dimension (Fig. 1). The lesion of GCM was a discrete mass without a capsule and composed of large polyhedral to elongated plump cells measuring about 30–40 μm in greatest diameter (Fig. 2B). Throughout the lesion the tumor cells were in close contact with each other, the elongated cells tending to form strands and whirls. The cytoplasms were finely granular and eosinophilic by H&E staining, and were positively stained by PAS staining after diastase digestion. Bodian's silver staining demonstrated a few fine elastic fibers surrounding many of the tumor cells.

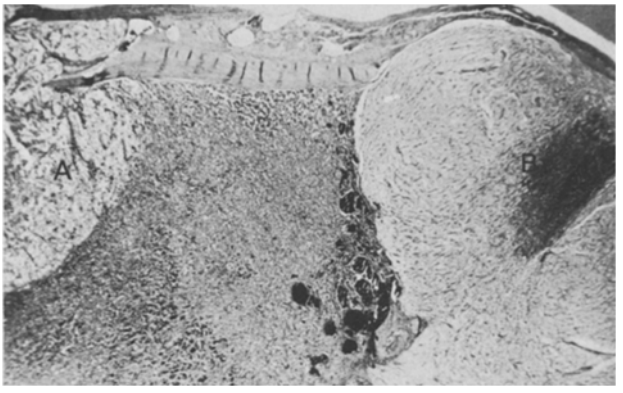

Fig. 1. The anterior (*left*) and posterior (*right*) lobes of the pituitary gland contained a chromophobe adenoma (*A*) and a GCM (*B*), respectively, in close contact with the fibrous capsule. × 14

Immunocytochemical Findings

The adenoma cells in anterior lobe did not exhibit massively immunoreactive cytoplasms to GH, PRL, TSH, LH, or FSH (Fig. 3A–E). At the periphery of the tumor were scattered neoplastic cells positive for GH and PRL (Fig. 3A, B). A few cells positive to TSH, LH, and FSH were also intermingled in the transition zone of the tumor (Fig. 3C–E). A few scattered cells positive to GH, PRL, or LH were also observed in mid portion of the tumor.

Electron-microscopic Findings

The electron micrographs of GCM revealed membrane-bound granules of various shapes and sizes. These granules were composed of round granular bodies varying from dense to light electron density. Occasional irregularly laminated masses were also observed.

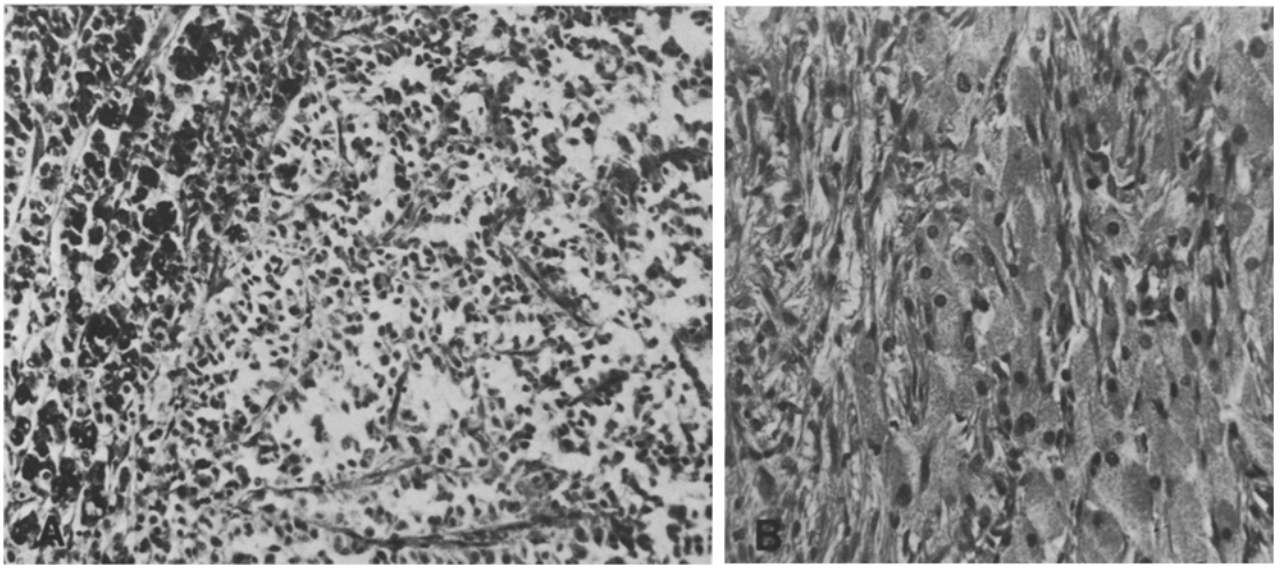

Fig. 2. A chromophobe adenoma (**A**) consisted of trabecullar to sinusoidal patterns up to a few cell layers and gradually transformed to the normal gland (*left side*) by a pushing margin. A lesion of GCM (**B**) consisted of polygonal to elongated granular cells with plump cytoplasms and round nuclei. × 140

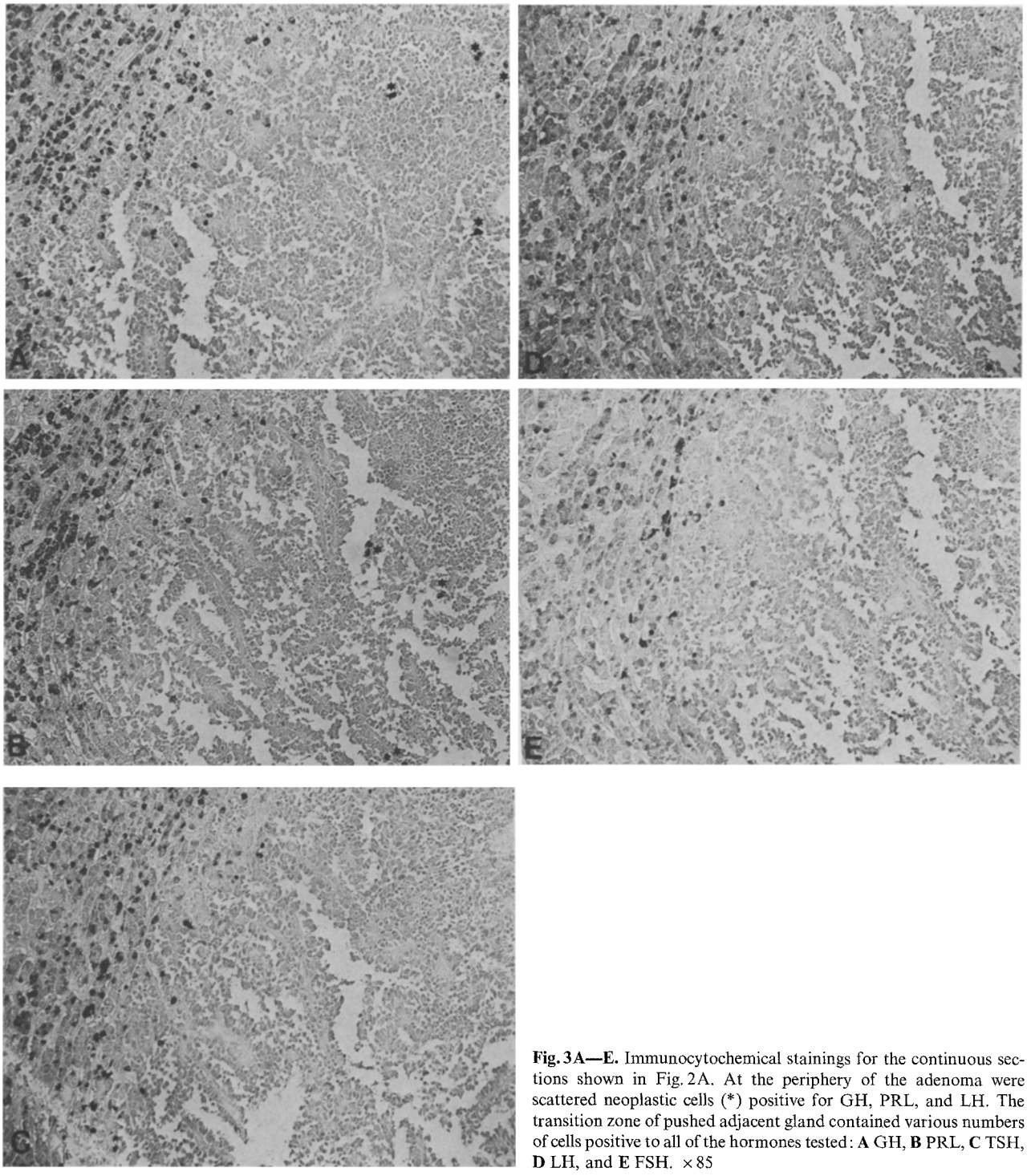

Fig. 3A—E. Immunocytochemical stainings for the continuous sections shown in Fig. 2A. At the periphery of the adenoma were scattered neoplastic cells (*) positive for GH, PRL, and LH. The transition zone of pushed adjacent gland contained various numbers of cells positive to all of the hormones tested: **A** GH, **B** PRL, **C** TSH, **D** LH, and **E** FSH. ×85

Discussion

PRL production by chromophobe adenomas is common as shown in this case. Scanarini et al. (1979) estimated that immunoreactive PRL was present in about 50% of the pituitary adenomas, whereas true chromophobe adenomas were about 5% (Muller et al. 1980). The coexistence of PRL and GH containing cells were described in the tumors from acromegalic patients (Ontjes et al. 1976). The presence of neoplastic TSH-containing cells were also reported in acidophilic-chromophobic tumors (Horn et al. 1970) and in chromophobe tumors (Bayliss 1976). GH-PRL-ACTH-secreting adenoma was also reported (Scanarini

et al. 1979). By tissue culture of resected pituitary adenomas, secretion of GH and PRL were elucidated by the same tumor (Marhiter et al. 1979). A small amount of LH and TSH secretion was also reported in addition to the major secretion of GH (Kohler et al. 1969). The peripheral zone of the present case revealed some neoplastic cells positive to five different anterior pituitary hormones tested. Thus, it is conceivable that these tumor cells may well secrete multiple hormones if incubated in vitro in response to the adequate secretagogues. The precursor cells common to all APUD (amine precursor uptake and decarboxylation) cells including anterior pituitary cells, can be altered by modulating enzymes, to one or more of a spectrum of peptide hormones (Lips et al. 1978). With abnormal growth, multipotential precursor cells could express one or more of their morphologic and functional possibilities (Tomita et al., in press). Furthermore, recent study suggests the presence of common precursor molecule of ACTH and endorphin (Eipper and Mains 1980). This supports the possibility of more than one hormone elaborated by one type of pituitary cells although the concept of one-cell-one-hormone has been widely accepted to date (Baker 1979).

The origin of GCM of the neurohypophysis is a matter of controversy. GMC was initially thought to be derived from myxoid cells (Abrikossoff 1926; Murray 1951). The possible origin has further extended to include: perineural fibroblasts (Pearse 1950), histiocytes (Ishii et al. 1977), Schwann cells with histiocytic properties (Fisher et al. 1962), oncocytes (Hamperl 1936), and primitive mesenchymal cells (Sobel et al. 1973). In regard to histogenesis of GCM in neurohypophysis, Rubinstein (1972) and Ulrich et al. (1974), suggested that it originates in the neuroglia and thus is of neuroectodermal origin.

In our case GCM of neurohypophysis was accompanied by a chromophobe adenoma of adenohypophysis. It may be further speculated that these tumors are derived from the common neuroectodermal cells with capacity to differentiate into anterior and posterior pituitary cells (Pearse 1977).

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