Diagnosis and management of prolactinomas

James R. Dollar & Richard E. Blackwell
Department of Obstetrics and Gynecology University of Alabama at Birmingham

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Abstract

Prolactin secreting tumors account for ten to twenty percent of all intracranial lesions. The patients harboring these tumors present with amenorrhea, galactorrhea, other ovulatory disorders, infertility, delays in puberty and mixed polyendocrinopathy. These tumors are diagnosed by the measurement of serum prolactin levels, Goldmann-Bowl perimetry, and either computed axial tomography or magnetic resonance imaging. Protein secreting tumors are usually benign lesions and historically have been treated by partial or total hypophysectomy or radiation therapy. Surgical resection of the lesion often is followed by recurrence and administration of proton beam radiation therapy results in the development of a panhypopituitary state. Growth of pituitary tumors is controlled with the administration of dopamine agonists such as bromocriptine and prospective studies have suggested that these drugs are now the preferred method of treatment for primary lesions and recurrences.

Introduction

Prolactin secreting tumors account for ten to twenty percent of all intracranial lesions. While adenomas seldom lead to death, their presence is associated with amenorrhea, galactorrhea, visual disturbances, headache, infertility, delayed puberty and polyendocrinopathy are associated with the presence of an adenoma (1). The introduction of computerized axial tomography, prolactin radioimmunoassay and dopamine agonists such as Parlodel during the last fifteen years has increased our ability to diagnose and treat prolactinomas (2). This review will discuss the features of prolactinomas, their possible etiology, diagnosis and treatment of these lesions, and current trends in prolactin research.

Anatomy

The pituitary gland is a unique structure composed of two different tissue types. The posterior portion of the gland develops from neuroectoderm while the anterior hypophysis arises from an outpocketing of the embryonic Rathke’s pouch. The anterior pituitary consists of three classes of cells, chromphobes, acidophils and basophils. These cell types can be differentiated on the basis of their staining with H&E or PAS. Recently immuno-
chemical and microscopic techniques have been developed which allow for the identification of cells secreting specific peptide hormones. Each trophic hormone appears to be the product of a distinctly different cell type (3).

Pituitary adenomas are derived from one of three cell types. The basophilic adenoma is a rare lesion and is associated with the secretion of either ACTH or b-MSH. The acidophilic adenoma comprises 10% to 15% of pituitary adenomas and has been found to secrete either growth hormone and/or prolactin. Chromophobe adenomas account for 85% to 90% of all pituitary lesions and have been associated with the secretion of prolactin, growth hormone, ACTH and/or b-MSH. Any of these tumors can be of the non-secretory type and thus asymptomatic. Such lesions will present with identical findings at autopsy. Pituitary adenomas are generally classified as either microadenoma (less than 1 cm in diameter) or macroadenoma (greater than 1 cm in size). The term ‘invasive adenoma’ has been applied to rare forms of macroadenoma which show more bizarre cell structure.

Incidence of adenomas

The incidence of prolactinomas is not known, however in 1936 Costello evaluated 1000 pituitary glands obtained at unselected autopsy. He found a 25% incidence of the presence of pituitary tumors in the glands with 60% of the lesions occurring in males and 40% in females (4). The advent of prolactin radioimmunoassay and more sensitive radiographic imaging techniques has increased our ability to diagnose the presence of the prolactinoma. Current estimates of the annual incidence rate of prolactinomas has increased from 1 to 7 per 100,000 women. However, since only symptomatic individuals are investigated for the presence of prolactinomas, it is probable that many of these lesions go undiagnosed and are asymptomatic. It is also probable that many adenomas that do not secrete trophic hormones escape detection and it is also possible that many of these lesions develop and regress without producing any signs or symptoms. However, if the tumors secrete biologically active hormones, their effects can produce dramatic alterations in phenotype, resulting in such disorders as Cushing’s syndrome or acromegaly.

Natural history of prolactinomas

The etiology of prolactinomas is unclear. It has been suggested that these lesions may be multifocal and result from a disorder of dopamine metabolism. Following surgical or medical therapy for prolactinomas, individuals harboring these lesions appear to have disorders of central dopamine synthesis and secretion. Since prolactin is unique among the pituitary trophic hormones in being tonically inhibited by dopamine, a disturbance in the metabolism of this neurotransmitter would result in an unopposed rise in prolactin secretion (5). Further, when one considers that the anterior pituitary has a bilobe configuration with each compartment receiving separate blood supply, an alteration in either blood flow from the median eminence or in the concentration of dopamine being delivered to that area of the gland might explain the unilateral occurrence of these lesions. Regardless of the origin of the lesion, dopamine appears to regulate both the synthesis and secretion of prolactin (6). Once the inhibitory influence of dopamine is removed from the gland, functional hyperplasia occurs and cells are demonstrated to have increased secretory activity (Fig. 1). These cells do not appear to acquire autonomous function and will respond to stimulators and inhibitors of prolactin secretion such as thyrotropic releasing hormone, dopamine, dopamine agonists and estrogens, in an appropriate manner. The behavior of such tumors in vivo seems to correlate with such in vitro observations (7). Regardless of whether the tumor is classified as micro- or macroadenoma, it generally decreases in size and biological activity when exposed to a dopamine agonist. Following discontinuation of the inhibitor, these lesions rapidly regain their original size and resume prolactin synthesis and secretion (8). Therefore, these tumors behave more like hyperplasias found in other organ systems and it has been proposed that disorders of central dopamine metabolism may give rise