CASE REPORTS

Prolactinoma with Extensive Amyloid Deposits: a Case Report

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Prolactinomas are common benign pituitary neoplasms. Amyloid deposits are rare findings that have been reported in pituitary neoplasms. We report a case of a 48-year old man with a diagnosis of prolactinoma with extensive amyloid deposition. To our knowledge, this is the first case of amyloid in a pituitary neoplasm at our institution.

Key words: Pituitary adenoma, Prolactinoma, Amyloid deposits

Prolactinomas are benign pituitary neoplasms producing prolactin. They are the most common form of pituitary neoplasms and represent the most common cause of hyperprolactenemia. Most of them arise in women of reproductive age. The male/female ratio is 1:2.6 (1). The etiology of prolactinoma is unknown. Clinical manifestations vary with patient's sex and age and tumor size (2). In men, they are often functionally silent, coming to the clinical attention at the macroadenoma stage with signs and symptoms of hypopituitarism, symptomatic compression of the visual system, and invasion into adjacent structures (3). On histologic examination, 10% of prolactinomas show psammomatous calcifications, a characteristic that is rare in other types of pituitary adenomas. Far less frequent is the presence of amyloid deposition (3-7). Amyloid has been reported to be present in various types of tissues; liver, spleen, kidney and the intestines are among them. Also, amyloid accumulation has been reported in endocrine organs such as pancreatic islets of Langerhans, thyroid and pituitary gland. Hyaline bodies which were interpreted to be due to progressive degeneration of adenoma cells were first reported by Ribbert in 1882. Barr and Lampert were the first describing, with uncertainty, the presence of pituitary neoplasm bodies composed of amyloid. In 1975, independent studies examined surgical specimen that found to have amyloid deposits (4-5). Still, it was not until 1983 when a prolactin-secreting pituitary adenoma was proven to contain amyloid substance (6). Dopamine agonists such as bromocriptine and cabergoline have changed the treatment of symptomatic prolactinomas. In approximately 66% of patients, tumor size will be reduced by as much as 75%, especially in those with large tumors (8). Treatment with bromocriptine has been associated to extensive tumoral fibrosis and amyloid formation (9-13).

We describe the case of a 48-year old man with a diagnosis of prolactinoma with amyloid deposition. The light microscopy and immunohistochemical characteristics of the neoplasm are discussed.

Case Report

A 48-year-old man was seen for the first time in October 2005, by the neurosurgeon, for a 2-month history of progressive blurred vision (mainly right eye). Examination was unremarkable, except for a left homonymous hemianopsia. At the time, hormonal analysis was as follow; prolactin (PRL) levels 16,980 ng/ml (nl <25 ng/ml), fasting growth hormone (GH) 1.3 ng/ml (nl <5 ng/ml), luteinizing hormone (LH) 1.72 mIU/ml (nl 6-23 mIU/ml), follicle stimulating hormone (FSH) 2.19 mIU/ml (nl 4-25 mIU/ml), free T4 6.2 mcg/dl (nl 5-12 mcg/dl) and morning cortisol 0.63 mcg/dl (nl 5-30 mcg/dl). Magnetic resonance image (MRI) study showed high signal intensity mass arising from the pituitary gland, with parasellar and suprasellar extensions, compressing the optic chiasm and revealing a cystic component (Figure 1A and 1B). He was placed on Parlodel® 10 mg BID for the following 3 months. In view of no clinical or imaging improvement and despite decrease of prolactin levels (168 ng/dl), the patient was admitted on January 2006 for elective surgery.

Surgical procedure

A right fronto-temporal craniotomy with microsurgical subtotal resection was performed. Intraoperatively, various

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small, yellowish, spherical masses were noticed (Figure 2). Surgery went without complications.

Postoperatively, the patient developed respiratory failure, panhypopituitarism, acute renal failure, Steven Johnson Syndrome and sepsis. A month and a half after hospitalization the patient died of his complications. An autopsy was performed.

Pathologic findings

Hematoxylin and eosin staining revealed a monotonous population of round to polygonal cells with round to oval nucleus and variable amount of eosinophilic cytoplasm (Figure 3A). The cells were arranged in sheets with intervening vascularized fibrous stroma. Mitoses were absent. Reticulum stain showed a disruptive reticulum pattern consistent with adenoma. Immunoperoxidase staining demonstrated that adenoma cells were immunoreactive for prolactin. A striking feature on light microscopic examination was the presence of masses of spherical, laminated, slightly eosinophilic material (Figure 3B). This material stained positively and showed birefringence under polarized light with Congo red stain (Figure 3C).

Discussion

Amyloid deposition has been associated to a great variety of conditions both systemic and localized. Localized endocrine amyloid deposits, as those seen in pituitary gland, are also termed APUD (ammine precursor uptake and decarboxylation) amyloid because the cells that secrete it share the property to handle precursors of biogenic amines (7). These deposits may be different from amyloid in other endocrine tissues (14).

Amyloid deposits in pituitary adenoma are of two types: stellate perivascular and spheroid. The first form is more frequent, has a fibrillary or crystalloid microstructure, and is found along blood vessels. The second form consists of an accumulation of coral-like spheres (7, 12). The pathologic findings in this case showed the spheroid type of amyloid deposits which is rare and is associated almost exclusively to prolactinomas (7).

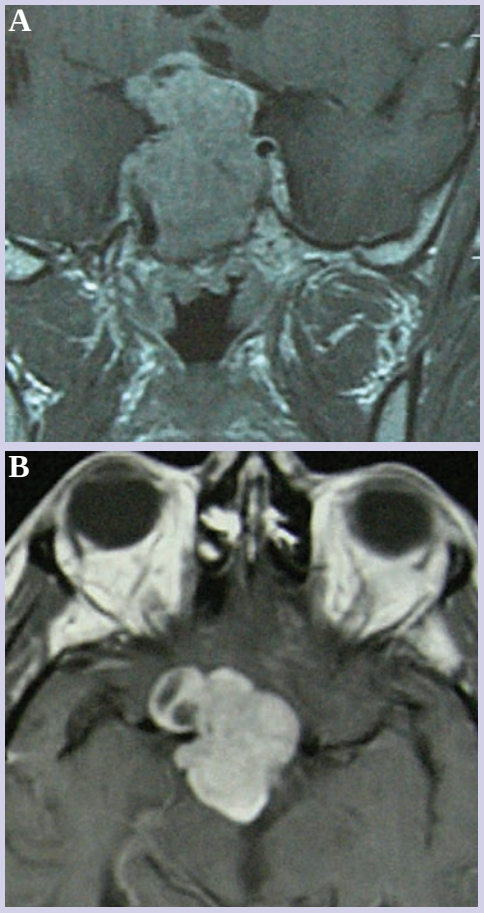

Figure 1. Brain MR T1-weighted images (A) Coronal, (B) Axial reveal a high signal pituitary cystic mass with suprasellar and parasellar extension, and compression of the optic chiasm

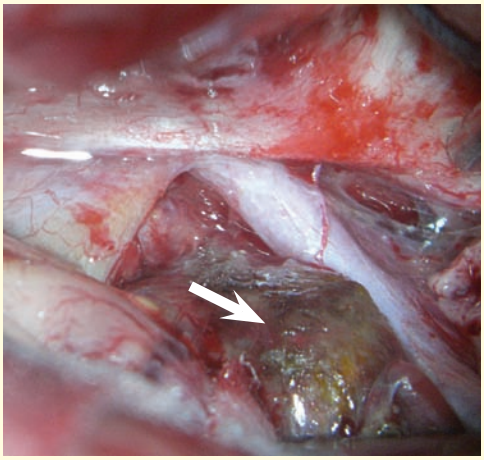

Figure 2. Intraoperative examination found various small, yellowish, spherical masses (arrow) within the adenoma.

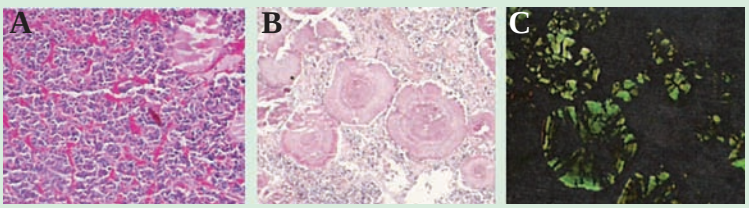

Figure 3. (A) Hematoxylin and eosin staining revealed a monotonous population of round to polygonal cells with round to oval nucleus and variable amount of eosinophilic cytoplasm. The cells were arranged in sheets with intervening vascularized fibrous stroma. Mitoses were absent. This material stained positively (B) and showed birefringence under polarized light (C) with Congo red stain.

The origin of the amyloid deposits in prolactinomas is not well established. It has been postulated that the amyloid fibrils are produced by adenoma cells, possibly during their degeneration (13). Another suggested possibility is that mesenchymal histiocytes produce the amyloid by an unknown process (6, 13, 15). Hinton D, et al. characterized the spherical amyloid protein from a prolactinoma and demonstrated that it is a 4 kDa peptide composed of N-terminal aminoacids 1-34 of prolactin (16). They concluded that intact prolactin is being abnormally processed in the formation of spherical amyloid (16). Long term treatment of prolactinomas with bromocriptine often results in extensive tumoral fibrosis (9-11). It has also been suggested that amyloid accumulation is enhanced in adenomas treated with bromocriptine (12-13).

From January 2002 to May 2006, 111 cases of pituitary lesions were operated at our institution, 3 of which were prolactinomas. All prolactinomas and most pituitary neoplasms have been diagnosed by a neuropathologist. To our knowledge this is the first case of prolactinoma with extensive amyloid deposition diagnosed at our institution. The clinical and pathologic findings were discussed along with a review of the pertinent literature. We were not able to determine the origin of the amyloid deposits or if previous bromocriptine treatment influenced amyloid accumulation in this patient. Neither, we were able to establish if prolactinomas operated before January 2002 were positive for this rare finding.

Resumen

Los prolactinomas son neoplasias comunes de la glándula pituitaria. Los depósitos amiloideos son hallazgos infrecuentes que han sido reportados en la literatura. Nosotros presentamos un paciente masculino de 48 años de edad con diagnóstico de prolactinoma y acumulación amiloidea. Para nuestro conocimiento, este es el primer caso de neoplasia de la pituitaria con material amiloideo en nuestra institución.

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