CASE REPORT

Extensive spherical amyloid deposition presenting as a pituitary tumor

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ABSTRACT. A 71-yr-old man was admitted for further evaluation and trans-sphenoidal surgery of a pituitary tumor. He complained of impotence and decreased libido over a period of about 40 yr. Thirty-eight yr ago he was treated for bilateral gynecomastia with galactorrhea. Endocrinological investigation at presentation revealed only mild hyperprolactinemia and hypogonadotropic hypogonadism. Pituitary magnetic resonance imaging (MRI) showed a tumor up to 2.5 cm in diameter with infiltration of the sphenoid sinus and right cavernous sinus. The tumor exhibited a heterogeneous hyperintense signal on T1-weighted images and hypointense signal on T2-weighted images. Standard trans-sphenoidal surgery was performed and a brownish mass was found inside the sella, which was removed. Histological examination of

INTRODUCTION

Extensive intrasellar spherical amyloid deposition is a rare finding in pituitary adenomas, with less than 20 cases reported up to today (1). Spherical amyloid deposition is almost exclusively encountered in PRL producing pituitary adenomas and only exceptionally occurs in GH and ACTH secreting or inactive adenomas (1). Abnormal processing of a hormone or prohormone by the adenoma cells has been suggested as the origin of the spherical amyloid formation (2). Amyloid deposits do not cause any charac-

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the mass revealed extensive spherical amyloid deposits with strongly positive immunohistochemical staining for prolactin. Therefore, a prolactinoma with extensive spherical amyloid deposition was diagnosed. Extensive spherical amyloid deposition is a rare finding in prolactin-secreting pituitary adenomas. So far, characteristic radiological findings by MRI have been described only twice. Due to characteristic MRI findings, the diagnosis of extensive intrasellar amyloid deposition can be entertained pre-operatively. Trans-sphenoidal surgical resection is essential to confirm the diagnosis histologically and because of the potential lack of tumor shrinkage under dopaminagonist therapy in this type of prolactinoma.

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teristic clinical or biochemical features. Therefore, intrasellar amyloid deposition is not usually recognized pre-operatively. Magnetic resonance imaging (MRI) of intrasellar amyloid deposits have been described only twice (3, 4).

We report a patient who was admitted for further evaluation and trans-sphenoidal surgery of a pituitary tumor. Intra-operatively, parts of the sphenoid sinus and the sella were filled with a brownish waxlike mass of soft consistency. The histological investigation of this mass revealed almost exclusively spherical amyloid bodies.

CASE REPORT

A 71-yr-old man was referred for further evaluation for an incidentally found pituitary tumor on a computed tomography (CT), which was performed due to a syncope. The patient had had impotence and decreased libido for about 40 yr, but attributed them

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to psychosocial factors. Bilateral mastectomy due to gynecomastia and galactorrhea was performed 38 yr ago. Laboratory results from that time were not available. Arterial hypertension was treated with a β blocking agent. Physical examination disclosed peripheral neuropathy with absence of ankle jerks and impaired vibratory sense. The rest of neurological examination was normal including normal visual fields. Testes were soft, 14 and 10 ml in volume. Skin was pale and showed fine wrinkles in the corners of the eyes and mouth. Body and facial hair was sparse, and pubic hair showed a female distribution pattern (Tanner P4-P5) suggesting hypogonadism.

Laboratory investigations showed mildly elevated prolactin levels of 72.5 μ g/l (normal 2.2-18.5). Total T was low at 2.5 nmol/l (reference 8.2-35) and free T was 7.2 pmol/l (reference 19-66 for men above 60 yr). FSH and LH serum levels were in the normal range (LH 2.4 IE/l, reference 2-12 and FSH 4.9 IE/l, reference 2-12). Thyroid indices were normal and

serum cortisol level of 480 nmol/l (reference 280-690 nmol/l), drawn at 08:00 h confirmed a normal adrenal function. The IGF-I was low at 48 μ g/l (reference for adults 100-300 μ g/l). Routine hematological and chemical parameters including inflammatory markers were within the normal range. Pituitary MRI demonstrated a sellar mass of 2.5 x 1.8 x 1.8 cm diameter, without suprasellar extension but with infiltration of the sphenoid sinus and right cavernous sinus (Fig. 1). The pituitary stalk was shifted to the left side. This tumor mass showed

heterogeneous hyperintensity on T1-weighted images without iv contrast (Fig. 1A) and was hypointense on T2-weighted scans (Fig. 1D).

After a trans-nasal/trans-sphenoidal access to the sphenoid sinus, the sphenoid mucosa was found to be normal, but the sellar floor was penetrated by a brownish, soft and wax-like, slightly dotted mass. Exploration of the sella revealed no classical pituitary adenoma. The tumor was re-



Fig.1 - MRI findings. Sagittal (A) and coronal (B) T1-weighted MR images without iv contrast showing the heterogeneously hyperintense mass (arrow). On coronal T1-weighted MR images with iv contrast, the mass is hypointense in comparison with the hypophyseal tissue (arrow) (C). On T2 coronal image (D) the mass is strongly hypointense as compared to the brain parenchyma.

moved by ring curettes. The compressed pituitary gland was pushed to the left side of the sella turcica. Tuberculosis, bacterial and mycotic infections were ruled out by negative microbiological investigations of the material (Gram-staining, culture and PCR). The post-operative course was uneventful.

Paraffin-embedded tissue sections stained with hematoxylin and eosin revealed that the removed mass was composed almost entirely of a spherical eosinophilic material. This amorphous material stained positively and showed birefringence under polarized light with Congo red, indicating that it represented amyloid (Fig. 2 A-D). Immunohistochemically, the extracellular amyloid spheroids were positive for prolactin (Fig. 2E). Staining for growth hormone, FSH, LH, TSH, ACTH and α subunit as well as for β -A4-amyloid was negative. Further investigation for systemic amyloidosis was



Fig. 2 - Pathology findings. The specimen consisted of several fragments of amorphous material. (A) Hematoxylin and eosin stained fragments of amorphous material consisting of numerous small concentric portions. In addition, there are small fragments of hypercellular tissue, which contain compressed pituitary as it can be appreciated upon reticulin silver staining (B). Congo red (C) strongly stains all the amorphous material that appears with green birefringence in polarized light (D). The amyloid stains positively for prolactin and negative for all other pituitary are positive for ACTH and negative for prolactin (F).

negative (transabdominal us, chest radiography and immunoelectrophoresis). Replacement therapy with testosterone was initiated postoperatively, and resulted in improved well-being. The serum prolactin level slightly decreased (63.5 μ g/l, normal 2.2-18.5) postoperatively and remained in this range at 1-yr follow-up. Repeat MRI of the sellar region showed tumor remnant.

DISCUSSION

We report a man with a large pituitary tumor containing mainly spherical amyloid deposits. The long history of impotence and decreased libido and the early occurrence of gynecomastia with galactorrhea were suggestive for hypogonadism due to prolactinoma. Compression and apoptosis of adenoma cells due to a local mass effect of the extensive intrasellar amyloid seem a possible explanation for the only mild hyperprolactinemia at diagnosis in described patient with long-standing disease. Immunohistochemical staining of the spherical amyloid deposits was strongly positive for PRL, indicating that the amyloid deposits were secreted directly by prolactin-secreting cells. In addition, extensive spherical amyloid deposition occurs typically in patients suffering from prolactinoma (5).

Two different histological patterns of amyloid deposits in pituitary adenomas have been described, the stellate and the spherical, respectively (6). Stellate amyloid is found perivascularly in a fibrillary pattern and small amounts may be frequently encountered in pituitary adenomas. No immunoreactive cytokeratin can be detected in these deposits. The type of spherical amyloid is rare. It is characterized by amorphous spheres adjacent to adenoma cells and containing immunoreactive cytokeratin fibrils. Extensive deposition of amyloid spheroids in a pituitary adenoma is uncommon. In our patient, the amyloid mass penetrated the sellar floor and extended into the sphenoid sinus. This behavior would be expected rather from a pituitary macroadenoma than from an amyloid mass.

Abnormal processing of prolactin or the prohormone produced by the adenoma cells rather than a mesenchymal origin as shown in other forms of systemic amyloidosis have been suggested as origin of the pituitary amyloid (2). This was concluded from the ultrastructural demonstration of amyloid fibrils within adenoma cells and the immunohistochemical positivity for prolactin of the amyloid deposits in some reported cases including described patient (7). Isolation and biochemical analysis of protein derived from spherical amyloid deposits in a prolactin-secreting pituitary adenoma disclosed an abundance of a 4-kDa peptide (8). Amino acid sequencing revealed that this amyloidogenic peptide represents the first 34 amino acids of the intact PRL protein.

On MRI, amyloid depositions in systemic amyloidosis usually show signal intensity similar to that of muscle on T1-weighted images and low to intermediate signal on T2-weighted images. The latter is the most characteristic feature of amyloid deposition (9). We found the same hypointense signal on T2-weighted images in our patient with intrasellar amyloid deposition, as described twice earlier (3, 4). These typical findings allow now suspecting intrasellar amyloid deposition even preoperatively. Patients with suspected intrasellar amyloid deposition in prolactin-secreting pituitary adenomas should be treated surgically in order to confirm the diagnosis histologically and to remove the intrasellar amyloid deposits due to the potential lack of tumor shrinkage under dopaminagonist therapy. Dopamin-agonist therapy may even increase the amyloid deposition (4, 5).

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