

Amyloidogenic Pituitary Prolactinoma

Pidakala Premalatha, Inuganti Venkata Renuka*, Thumma Rayapa Reddy, Akula Meghana

Department of Pathology, NRI Medical College, Mangalagiri, India

Email: prema_6649@yahoo.co.in, *repriya56@gmail.com, drreddythumma@gmail.com, megha348@gmail.com

Received 2 March 2016; accepted 27 May 2016; published 30 May 2016

Copyright © 2016 by authors and Scientific Research Publishing Inc.

This work is licensed under the Creative Commons Attribution International License (CC BY).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

Abstract

Prolactinomas are the most common benign pituitary neoplasms and the common cause of hyperprolactinemia. Most of them arise in women of reproductive age. In men, they are often functionally silent, but present with manifestations secondary to pressure effects when they become macro adenomas. We present a case of prolactinoma in a 54-year old male patient who presented with pressure effects because of the tumor, as head ache and bi-temporal hemianopsia. MRI Brain scan was done to identify the tumor. The patient underwent trans-sphenoidal resection of the pituitary macro adenoma. Histological examination revealed spheroid amyloid deposits, almost replacing the adenoma. No medical treatment was given but the tumor recurred after 6 months and a repeat surgery was done for total excision.

Keywords

Pituitary Adenoma, Prolactinoma, Amyloid

1. Introduction

Amyloid deposits are not uncommon in endocrine neoplasms and can also occur in pituitary tumors. They are relatively common in prolactinomas and less common, but can occur in growth hormone (GH)—and corticotrophin (ACTH)—secreting or nonfunctional adenomas. But spherical amyloid deposition is almost exclusive to prolactin (PRL)—producing pituitary adenoma. It has been suggested that abnormal processing of hormone or prohormone by the adenoma cells is the origin of the spherical amyloid formation [1].

Pre-operative recognition is not usual as amyloid deposits do not cause any characteristic clinical or biochemical features.

Pituitary macro adenomas are one of the more common abnormalities of the sellar region, but reports of such adenomas containing localized amyloid deposits are rare in literature [2]-[5]. We report a case of pituitary adenoma composed of amyloid tissue almost in its entirety.

*Corresponding author.

2. Case Report

A 54-year old male presented with headache of one year duration, recent onset of diplopia and visual field disturbances; identified as bi-temporal hemianopsia. Ophthalmic examination revealed diminished visual acuity in both eyes. Fundus examination showed no signs of optic atrophy.

Hormonal analysis revealed extremely elevated levels of serum prolactin of 4700 ng/mL (normal 4.04 - 15.2 ng/mL) and normal levels of growth hormone (GH) 1.3 ng/ml, luteinising hormone (LH) 1.72 mIU/ml, follicle stimulating hormone (FSH) 2.19 mIU/ml, free T4 6.2 mcg/dl and morning cortisol 0.63 mcg/dl.

MRI Brain in T2 weighted images revealed heterogenous hypo intense with central hyper intense irregular lobulated mass lesion in sellar and suprasellar lesion measuring $4.7 \times 3.8 \times 3.9$ cms. The lesion showed peripheral blooming on gradient recalled echo (GRE) with T1 hyper intensity (**Figure 1**). The lesion was compressing optic chiasma and displacing it superiorly and causing splaying of circle of Willis. It was also encasing bilateral cavernous internal carotid arteries. There were small parasellar extensions with heterogenous enhancement on contrast administration.

The patient underwent Trans-sphenoidal adenectomy resulting in removal of small friable, grayish white tissue bits and was replaced with abdominal fat. The post operative period was uneventful and the vision disturbances abated. No medical treatment was given. The prolactin levels were near normal at the time of discharge.

The tumor recurred after 6 months with symptoms of CSF rhinorrhoea, decreased vision and photophobia. He was found to be having elevated prolactin levels and recurrence of tumor; considered probably secondary to incomplete excision. A repeat surgery was done for total excision and on further follow up the patient was asymptomatic with normal prolactin and other hormone levels but persistent diminished vision.

3. Pathology

Gross: Received multiple grey white tissue bits altogether measuring $3 \times 2 \times 1$ cm.

Microscopy: Hematoxylin and eosin staining revealed a monotonous population of round to polygonal tumor cells with round to oval nuclei and variable amounts of eosinophilic cytoplasm. The cells were arranged in sheets with intervening vascularized fibrous stroma. Mitoses were absent. The striking feature within the tumor was the presence of masses of spherical, laminated eosinophilic material) that formed coral-like structures (**Figure 2**) which stained positively with Congo red and showed apple green birefringence under polarized light (**Figure 3**).

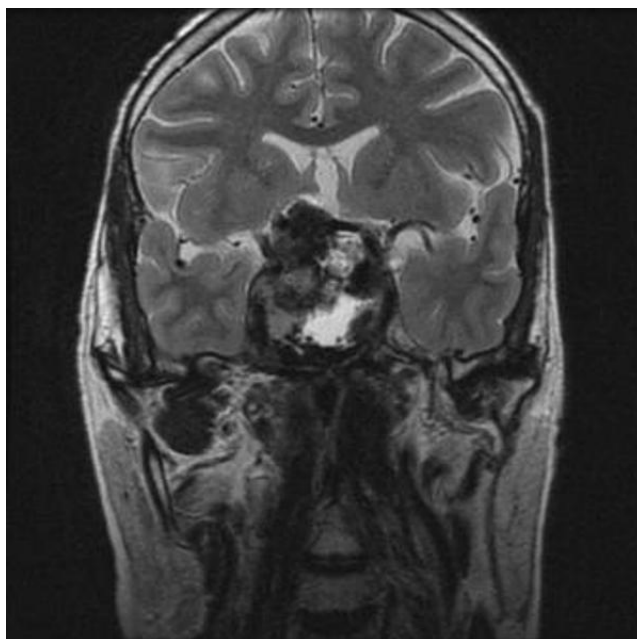


Figure 1. MRI scan in T2 weighted image showing heterogeneous hypo intense lesion with central hyper intense irregular lobulated mass in sellar and suprasellar location.

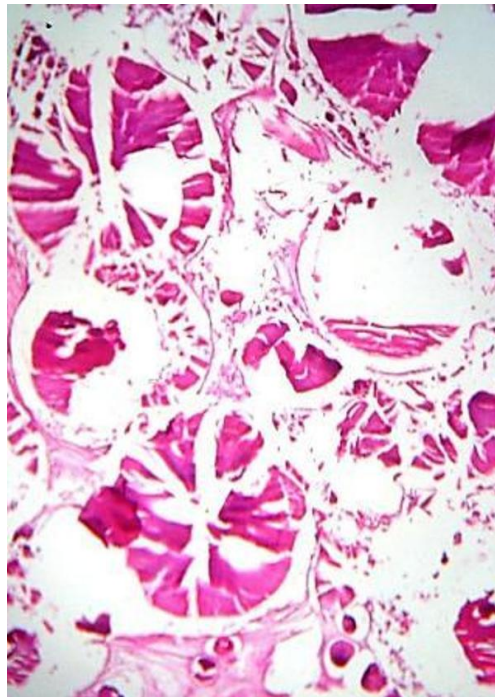


Figure 2. Microphotograph of tumor with masses of spherical, laminated eosinophilic amyloid material (H and E $\times 100$).

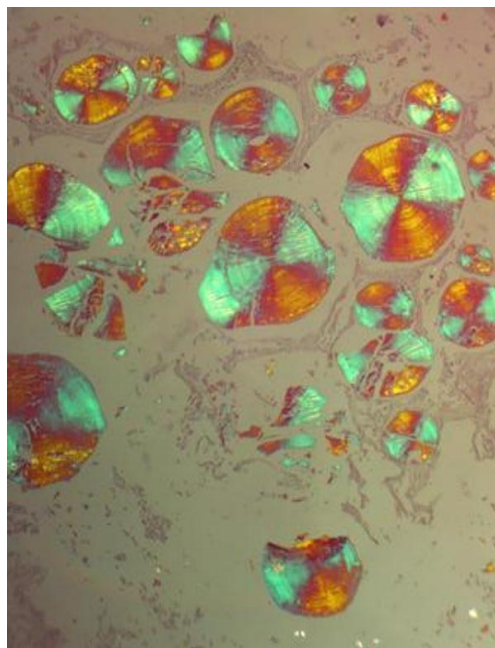


Figure 3. Congo red stain of tumor showing apple green birefringence under polarized light (Congo red $\times 100$).

4. Discussion

Pituitary macro adenomas are among the more common abnormalities of the sellar region and account for 10% - 15% of intracranial tumors. They originate within the anterior pituitary and usually are nonfunctioning [2].

Amyloid deposition has been associated with a great variety of conditions, both systemic and localized.

Localized endocrine amyloid deposits, as those seen in pituitary gland, are also termed APUD (amine precursor uptake and decarboxylation) amyloid because the cells that secrete it share the property to handle precursors

of biogenic amines [3]. These deposits may be different from amyloid in other endocrine tissues [2].

Only 13 cases of pituitary adenomas with localized amyloid deposits have been reported in the literature. The incidence varies among the different hormone-secreting types of adenoma and is highest in those secreting growth hormone and prolactin [2].

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 around blood vessels seen in many hormone producing tumors. The second form consists of an accumulation of coral-like spheres [3] [4]. The pathologic finding in this case showed the spheroid type of amyloid deposits which are rare and are almost exclusive to prolactinomas [5] [6].

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 [7].

Another suggested possibility is that mesenchymal histiocytes produce the amyloid by an unknown process [5]. Hinton D.R. *et al.* characterized the spherical amyloid protein from a prolactinoma and demonstrated that it is a 4 kDa peptide, composed of N-terminal amino acids 1 - 34 of prolactin. They concluded that intact prolactin is being abnormally processed in the formation of spherical amyloid [6]-[8].

A study by Saitoh *et al.* suggests that the degradation of secretory granules in vesicles containing amyloid fibrils seems at least partly responsible for the formation of amyloid [9]. This study also revealed that amyloid accumulation is enhanced in adenomas treated with bromocriptine compared with those not treated by this drug. Long term treatment of prolactinomas with bromocriptine often also results in extensive tumoral fibrosis.

5. Conclusion

Pituitary adenomas with coral like amyloid deposits are rare and found to be exclusive to prolactinomas. This was the first case of prolactinoma with extensive amyloid deposition diagnosed at our institute that showed recurrence subsequently. 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 in our patient and there was no history of bromocriptine treatment. The follow-up of the case was uneventful. We are reporting this case for its rarity.

References

- [1] Gul, S., Bahadir, B., Dusak, A., Kalayci, M., Edebalı, N. and Acikgoz, B. (2009) Spherical Amyloid Deposition in a Prolactin-Producing Pituitary Adenoma. *Neuropathology*, **29**, 81-84. <http://dx.doi.org/10.1111/j.1440-1789.2008.00922.x>
- [2] Bononi, P.L., Martinez, A.J., Nelson, P.B. and Amico, J.A. (1993) Amyloid Deposits in Prolactin Producing Adenoma. *Journal of Endocrinological Investigation*, **16**, 339-343. <http://dx.doi.org/10.1007/BF03348851>
- [3] Landolt, A.M., Kleihues, P. and Heitz, P.U. (1987) Amyloid Deposits in Pituitary Adenomas. *Archives of Pathology & Laboratory Medicine*, **111**, 453-458.
- [4] Molitch, M.E., Elton, R.L., Blackwell, R.E., *et al.* (1985) Bromocriptine as Primary Therapy for Prolactin-Secreting Macroadenoma: Results of a Prospective Multicenter Study. *The Journal of Clinical Endocrinology & Metabolism*, **60**, 698-705. <http://dx.doi.org/10.1210/jcem-60-4-698>
- [5] Kubota, T., Kuroda, E., Yamashima, T., Tachibana, O., Kabuto, M. and Yamamoto, S. (1986) Amyloid Formation in Prolactinoma. *Archives of Pathology & Laboratory Medicine*, **110**, 72-75.
- [6] Hinton, D.R., Polo, R.K., Linse, K.D., Weiss, M.H., Kovacs, K. and Gamer, J.A. (1997) Characterization of Spherical Amyloid Protein from a Prolactin Producing Pituitary Adenoma. *Acta Neuropathologica*, **93**, 43-49. <http://dx.doi.org/10.1007/s004010050581>
- [7] Saitoh, Y., Mori, H., Matsumoto, K., Ushio, Y., Hayakawa, T., Mori, S., Arita, N. and Mogami, H. (1985) Accumulation of Amyloid in Pituitary Adenomas. *Acta Neuropathologica*, **68**, 87-92. <http://dx.doi.org/10.1007/BF00688628>
- [8] Barrow, D.L., Tindall, G.T., Kovacs, K., *et al.* (1984) Clinical and Pathological Effects of Bromocriptine on Prolactin-Secreting and Other Pituitary Tumors. *Journal of Neurosurgery*, **60**, 1-7. <http://dx.doi.org/10.3171/jns.1984.60.1.0001>
- [9] Mori, H., Mori, S., Saitoh, Y., *et al.* (1985) Effects of Bromocriptine on Prolactin-Secreting Pituitary Adenomas. *Cancer*, **55**, 96-102. [http://dx.doi.org/10.1002/1097-0142\(19850101\)55:1<96::AID-CNCR2820550116>3.0.CO;2-2](http://dx.doi.org/10.1002/1097-0142(19850101)55:1<96::AID-CNCR2820550116>3.0.CO;2-2)