Case Report

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Silent Corticotroph Adenoma Presenting with Diabetes Insipidus: A Case Report

Sridhara Narayana Vuddagiri*, Alugolu Rajesh, Dinesh Shukla***, Megha Shantveer Uppin****, Challa Sundaram*******

Abstract

Background: Silent corticotroph adenoma (SCA) is a rare sub-type of non-functioning pituitary tumour and like other macroadenomas, they usually present with symptoms related to compression of the adjacent structures, but still *Diabetes insipidus* is rarely seen in SCA's. **Case report:** We report a 42 year old female presenting with left visual loss and *Diabetes insipidus* due to a silent corticotroph adenoma. **Conclusion:** SCA's have more aggressive course and increased rate of recurrence compared to other non-functioning tumors. *Diabetes insipidus* can rarely be associated with macroadenomas and thus such atypical presentation should also be kept in mind.

Keywords: Corticotroph adenoma; *Diabetes insipidus;* Silent; Pituitary.

Introduction

Silent corticotroph adenoma (SCA) is defined as pituitary adenoma with histological adrenocorticotrophic hormone (ACTH) immunoreactivity, without any clinical or laboratory evidence of elevated cortisol levels. The condition is uncommon with few case series having been reported. Unlike functional adenomas, patients with SCA usually come to medical attention secondary to compression of the adjacent structures. Pituitary adenoma presenting with *Diabetes insipidus* (DI) is very rare.The diagnostic dilemma on imaging and rare occurrences of SCA & DI together has prompted us to review the literature and report our case.

Case report

A 42 year old female presented to us with the chief complaints of gradually progressive, dull aching, bifrontal headache for approximately 6 months along with the history of progressive painless loss of vision in left eye for 5 months. Apart from polyuria and polydipsia her clinical history was unremarkable for any other endocrine disturbance. On examination her visual acuity was counting fingers at 2 meters in right eye with no perception of light in the left eye. Visual field analysis of right eye showed temporal field defect. Bilateral optic atrophy was noted on fundoscopy. She was investigated with MR imaging of brain, which showed a well defined sellar and suprasellar lesion of size 3x3x2cms, which was hypointense on T1 weighted imaging (T1W) with a central hyperintensity (Figure 1A) and on T2 weighted (T2W) images the lesion was hyperintense with a hypointensity with in it (Figure 1B). Lesion was seen extending superiorly into the suprasellar cistern compressing and displacing the optic chiasm and left optic nerve. On contrast administration the suprasellar part of the lesion was enhancing homogenously compared to the sellar part (Figure 1C & D). Our provisional diagnosis was sellar-suprasellar craniopharyngioma. The central hyperintensity on T1W image corresponding to the hypointensity on T2W image was thought to be due to the proteinaceous fluid with in

Author's Affiliation: *Senior Resident, **Assistant Professor, ***Assistant Professor, Department of Neurosurgery, ****Assistant Professor, *****Professor & Head, Department of Pathology, Nizam's Institute of Medical Sciences, Punjagutta, Hyderabad- 500082, India.

Reprint Request: Dr. A. Rajesh, M. S., M.Ch., Assistant Professor, Department of Neurosurgery, Nizam's Institute of Medical Sciences, Punjagutta, Hyderabad- 500082, India

E- mail: drarajesh1306@gmail.com

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Figure 1: MRI brain axial section showing a sellar-suprasellar lesion
(a) T1W image showing the lesion as hypointense with central hyperintensity

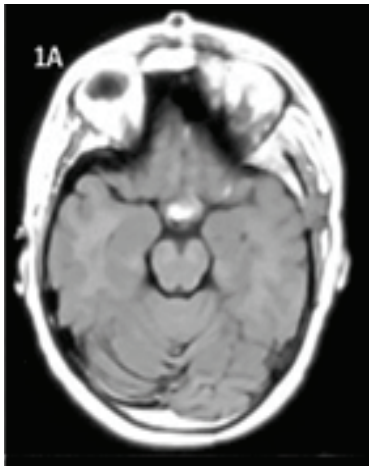


Figure 1 (b): On T2W the lesion is hyperintense with central hypointensity

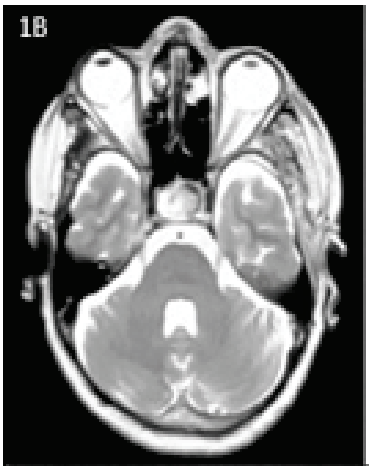


Figure 1(c): Lesion enhancing homogenously on contrast

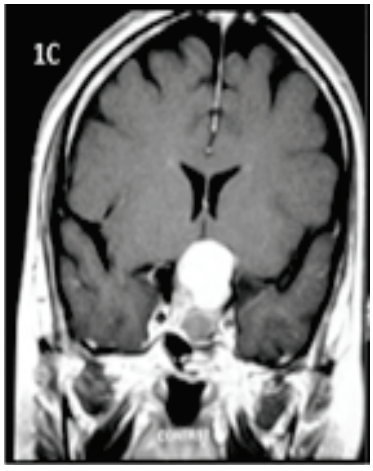


Figure 1 (d)

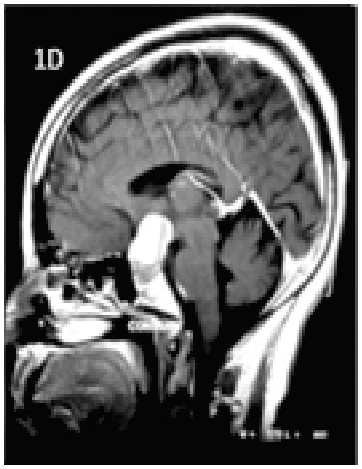


Figure 2 (a): Microscopic sections showing the loss of normal glandular pattern of the pituitary gland with neoplastic cells arranged in bands

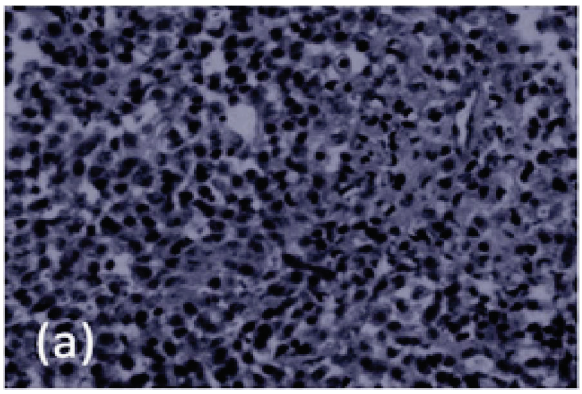
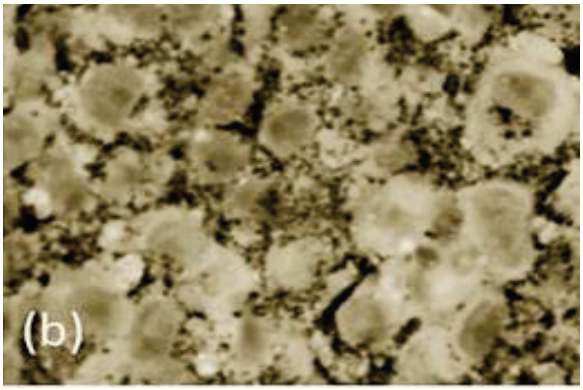


Figure 2 (b): IHC: Tumar cells showing strong immuno-reactivity to ACTH



craniopharyngioma. Hormonal analysis showed: Serum cortisol – 8 microgram/dl, Serum prolactin – 87 microIU/ml, FSH – 29 milliIU/ml, LH – 11 milliIU/ml, SerumT_3 – 1nmol/L, SerumT_4 – 5 microgram/dl,

serumTSH – 0.6 microIU/ml. Serum cortisol and prolactin were within normal limits, whereas the FSH, T_3, T_4 levels were low. Serum osmolality was 340 mosm/l (high), serum sodium - 152 meq/l (high) and urine osmolality was 150 mosm/l (low). We had not done serum ACTH levels since, the serum cortisol levels are within normal limits and there is no clinical suspicion of Cushing's disease. With the above findings a working diagnosis of craniopharyngioma with pan-

Table 1: Review of cases of silent ACTH adenoma

S. no	Author	Year	No. of patients	Clinical presentation	Imaging	Hormonal analysis	Per-op findings	HPE & IHC
1	Horvath *et al*[2]	1980	Total – 17 Males – 9/14 Females – 5/14	Headache – 21% Visual disturbances – 64% Endocrine disturbances – 7%	Macroadenomas – 78%	-	-	Moderate to strong ACTH reactivity.
2	Scheithauer *et al*[5]	2000	Total – 23 Males – 16 Females – 7	Headache – 50% Visual disturbances – 61% Endocrine disturbances – 43% Apoplexy – 9%	Macroadenomas – 100% Invasion – 50%	s.cortisol – normal – 100% Raised S.Prolactin – 21%		Moderate to strong ACTH reactivity.
3	Bradley *et al*[7]	2003	Total – 28 Males – 16 Females – 12	visual disturbances – 78.5%	Macroadenomas – 100% Invasion – 32%	-	-	-
4	Webb *et al*[6]	2003	Total – 27 Males – 8 Females – 19	Headache – 70.4% Visual disturbances – 55.6% Endocrine disturbances – 11.1% Apoplexy – 33%	Macroadenomas – 100% Invasion – 16%	S.Cortisol – normal – 100% S.Prolactin – 100% ACTH normal– 100%	Hemorrhage – 37%	ACTH strongly positive
5	Lopez *et al*[8]	2004	Total – 12 Males – 10 Females – 2	Headache – 8.3% Visual disturbances – 41.6% Endocrine disturbances – 33.3% Apoplexy – 16.6%	Macroadenomas – 91.6% Microadenomas – 9.4% Hemorrhage – 25%	s.cortisol – normal – 100% Raised ACTH – 5/10	-	-
6	Baldeweg *et al*[3]	2005	Total – 15 Males – 10 Females – 5	Headache – 13.3% Visual disturbances – 86.6%	Macroadenomas – 100% Invasion – 40% Hemorrhage – 40%	-	-	-
7	Sahli *et al*[4]	2006	Total – 4 Females – 4	Headache – 50% Visual disturbances – 25% Endocrine disturbances – 25%	Macroadenomas – 100% Hemorrhage – 50%	s.cortisol – normal – 50% Raised S.Prolactin – 50% Decreased gonadotropins – 50%		Angiomatous vessels seen in biopsy. ACTH strongly positive
8	Raverot *et al*[9]	2010	Total – 14 Males – 9 Females – 5	Headache – 28.5% Visual disturbances – 50% Endocrine disturbances – 21.4%	Macroadenomas – 100% Invasion – 7/9 patients. Hemorrhage – 7%	s.cortisol – normal – 100% Raised ACTH – 100%	-	ACTH strongly positive. Weakly positive in 1 case.
9	Ioachimescu *et al*[10]	2012	Total – 33 Males – 19 Females – 14	Headache – 30.3% Visual disturbances – 39.4% Endocrine disturbances – 39.4% Apoplexy – 9.1%	Macroadenomas – 100% Invasion – 45.5%	Raised S.Prolactin – 46.4% Single hormone deficiency – 42.4& Combined hormone deficiency – 33.3%	-	ACTH strongly positive – 57.5% Weakly positive – 42.5%
1o	Our case	2012	Female-1	Headache – present Endocrine disturbances - present	Macroadenoma Hemorrhage – present.	Combined hormone deficiency – present.		ACTH strongly positive

hypopituitarism was made. The patient was prepared preoperatively with supplementation of dexamethasone and thyroxine as hormonal stabilization. Since most of the tumor was located in the suprasellar region the tumor is approached transcranially. Tumor was grayish-yellow, soft, non-suckable, with a well defined capsule all around in the suprasellar area and undifferentiated from pituitary in the sellar portion, with a blood clot in it. No abnormal vessels were noted within the tumor intra operatively. She recovered well from the anaesthesia. Post operatively her visual status remained the same and diabetes insipidus has improved. Post operatively serum osmolality value has come down to 300 msom/l and urine osmolarity value has improved to 400 mosm/l. MRI showed minimal residual tumor attached to the stalk. Histopathological examination showed loss of the normal lobular pattern (Figure 2A) of the gland and strong positivity for cytokeratin and ACTH (Figure 2B). The Ki-67 was less than 1%.

Discussion

Silent pituitary adenomas are the non-functioning adenomas without any clinical or laboratory evidence of elevated hormonal levels but manifest histological immune-reactivity to the specific hormones. Yamada *et al* classified the non-functional adenomas into 7 morphological types[1] - null cell adenomas, oncocytomas, silent gonadotrophic adenomas, silent thyrotroph adenomas, subtype-I, subtype-II and subtype-III adenomas. Out of these subtypes, I & II are SCA's whereas type-III are of obscure origin. SCA show histologic ACTH immuno-reactivity without clinical or biochemical evidence of elevated cortisol levels. SCA's were first described by Horvath *et al*, in 1980.[2] Incidence of SCA is very low, accounting for only 5.6% of all pituitary adenomas in the case series of Horvath *et al*[2], whereas only 2.9% in Baldeweg et al[3] series (Table 1). No obvious sex predilection is noted as seen in Cushing's adenomas. Most of the studies have shown males to be more commonly affected than females but few studies have reported female preponderance. The median age of presentation was 40yrs from all the above cohorts. SCA's are endocrinologically non-functioning and the clinical manifestations are usually secondary to compression caused by the growth of the tumor, hence most SCA's present as macroadenomas.The most common manifestations of SCA are headache (20-70%) & visual disturbances (20-80%). Hypopituitarism leading to galactorrhea and amenorrhea is seen in 26% of patients. Hyperprolactinemia due to the stalk sectioning effect or tumoral endorphin secretion is about 11-43%. Pituitary apoplexy is more common in SCA when compared to functional ACTH adenomas. It is one of the major manifestations of SCA accounting for about 9-40%.The cause for this high frequency of apoplexy in SCA is not definitely established. Sahli *et al*[4] hypothesized that rupture of the prominent vessels present within the tumor to be the cause for hemorrhage. Our patient presented with headache, visual field deficits, pan hypopituitarism with mild elevation of serum prolactin levels and MRI showing altered signal intensity within the tumor, which was confirmed intra-operatively as altered blood, suggestive of an apoplectic event. All the manifestations of our patient are in concordance with the published literature, except for the *diabetes insipidus*. Pituitary adenomas presenting with *Diabetes insipidus* (DI) as the initial manifestation are very rare.DI is not the feature of subclinical corticotroph adenomas which occupy about 5% of so-called non-functioning adenomas. Clinically the presence of DI prompts a surgeon to suspect a craniopharyngioma or a Rathke's cleft cyst in the suprasellar region causing compression of anterior hypothalamus. Few case reports of pituitary abscess and pituitary metastasis causing *diabetes insipidus* have been published, but to our knowledge till now there is no case of silent corticotroph adenoma presenting as diabetes insipidus. Scheithauer *et al*[5] did not find any case with features of *Diabetes insipidus*. Our patient presented to us with headache and DI. Imageologically SCA's are indistinguishable

from functional ACTH adenoma, except for the larger size and high incidence of intratumoral bleed. By definition SCA is not associated with any excess in serum cortisol. Scheithauer *et al*[5] and Webb *et al*[6] have analyzed ACTH levels in 4 out of 27 SCA patients and 7 out of 23 SCA patients respectively and found it to be within normal limits. In our case ACTH levels were not analyzed. When compared to other non-functional adenomas, SCA's are more aggressive and have high recurrence rates. The importance of diagnosing SCA lies in its potentially aggressive clinical course and increased risk of recurrence following surgery. Bradley *et al*[7] diagnosed recurrences in 9 of their 28 SCA patients in the 5.8 yr follow-up. They concluded that the pre-operative invasiveness and the degree of ACTH immuno-reactivity did not predict tumor recurrence. They have advised to give radiotherapy following surgery in cases of incomplete resection, parapituitary invasion, or with aggressive features on histology, but with a word of caution to weigh the proven risks against unproven benefits of radiotherapy for non-functioning adenomas. Prophylactic radiotherapy can be avoided if regular follow-up with imaging is possible. In our case post operative radiotherapy was not suggested as there was no residual lesion and the proliferative index (Ki-67 <1%) was low. The patient is under constant follow up for eight months and post op MRI after 3 and 6 months did not show any recurrence.

Conclusion

Silent corticotroph adenoma is a uncommon variety of non-functioning pituitary adenoma and Diabetes insipidus as a manifestation of pituitary adenoma is quiet rare. Our case was a SCA with apoplexy having features of diabetes insipidus. SCA's have more aggressive course and increased rate of recurrence compared to other non-functioning tumors. So the importance of diagnosing SCA lies in its potentially adverse prognosis.

Abbrevations

Adrenocorticotrophic hormone (ACTH), *Diabetes insipidus* (DI), Silent corticotroph adenoma (SCA),

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