PITUITARY ADENOMA IN MEN1 AND OTHER ENDOCRINE NEOPLASIAS SYNDROMES P454

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Pituitary adenomas are usually sporadic, but can be observed in Multiple Endocrine Neoplasia type 1 (MEN1) or in the Carney's syndrome, Multiple Endocrine Neoplasias type 4 (MEN4) and in some hereditary pheochromocytomas/paragangliomas syndromes (HPPS).

AIM OF TH E STUDY

Analyze the frequency and characteristics of pituitary adenomas (PA) in classic and atypical MEN diagnosed between 1981 and 2013.

RESULTS

10 MEN were observed 6 MEN1 and 4 classified as atypical MEN either NEM4 or HPPS. PA were found in 8cases (80%): 4 associated to MEN1 and 4 to atypical MEN. 6/8 were macroadenomas (≥1cm) with invasiveness in 2 cases. Secreting adenomas were prevailing :5/8 = 62,5% (Table I).

	Case	Age	Sex	Secretion	Tumor Height (mm)	Treatment	Evolution	Associated Tumors
MEN1	1	59	M	Non secreting	7	Wait And See	Stable	Hyperparathyroidism (HPTH) +Pancreatic Tumor
	2	28	F	Nons ecreting	10	Wait And See	Stable	HPTH
	3	29	F	Prolactinoma	19	Bromocriptine	Tumor Reduction	HPTH
	4	56	M	Prolactinoma	50	Bromocriptine	Remission	HPTH
Atypical MEN	1	46	M	Non secreting	18	Bromocriptine	Stable	Paraganglioma (PGL)
	2	42	M	Gonadotroph adenoma (Fig.1)	21	Surgery	Increase (Ki67:5%)	PGL+ HPTH
	3	26	F	Somatotroph adenoma	25	Surgery Radiotherapy Lanreotide	Tumor Reduction	PGL+Rectal Carcinoid+HPTH
	4	57	F	Somatotroph adenoma	09	Surgery Radiotherapy Lanreotide	Remission	Adrenal Tumor+Thyroid Papillary Carcinoma + Renal Cyst+ Splenic Nodule+Ovarian Cystadenocarcinoma
	Total: 8 /10	Median Age: 42.87	4 F/ 4 M	5 secreting /3non secreting	Median Height: 19.88mm			Most common association: MEN 1:HPTH+ pituitary adenoma Atypical MEN:¾ PGL + Pituitary Adenoma

Aggressiveness (cavernous sinus invasion, poor response to medical treatment, high Ki67) was noted as total remission was observed in only 2 cases. In atypical MEN, PA were associated especially to paragangliomas.

DISCUSSION

PA are rare (10% of brain tumors) [1]. They are usually sporadic, but they can be part of hereditary syndromes such as MEN 1 (hyperparathyroidism, PA ± pancreatic or duodenal tumor). They may also be associated to neuroendocrine, adrenal and some non-endocrine tumors [2].

MEN1 is a very rare syndrome due to mutation of the MEN 1 gene encoding for Menine. MEN1 is rarely revealed by a PA contrary to what we observed. PA were observed in 4 of 6 MEN1= 66.6% vs 65% for Syro et al. [2]. In this study PA are represented by prolactinomas and non secreting adenomas.

Other cases(n=4) could fit into one of the following syndromes:

- MEN 4= New entity due to mutation of CDKN1B gene. MEN 4 patients can have MEN 1 like phenotype: the most common lesions are pituitary and parathyroid adenomas[3] . Other associated tumors may be testicular, pancreatic, thyroid, and neuroendocrine. Tumors located in the breast and uterus are also possible. Due to the limited number of reported cases, different characteristics of MEN 4 are not clearly established, especially for pheochromocytoma which is reported in the animal model with a complete penetrance. [3]

- Syndromic pheocromocytoma/paraganglioma: Three of our patients have PA adenoma associated to paraganglioma whose etiology could match MEN 4, but can also integrate HPPS. The association of a paraganglioma to a PA is rarely reported, but it is apparently caused by gene mutations: SDH (A [4], B, C or D [5]). The PA may be a somatotroph adenoma, a non secreting (as in our patients) or a prolactinoma. But, only an enlarged genetic study can confirm this entity.

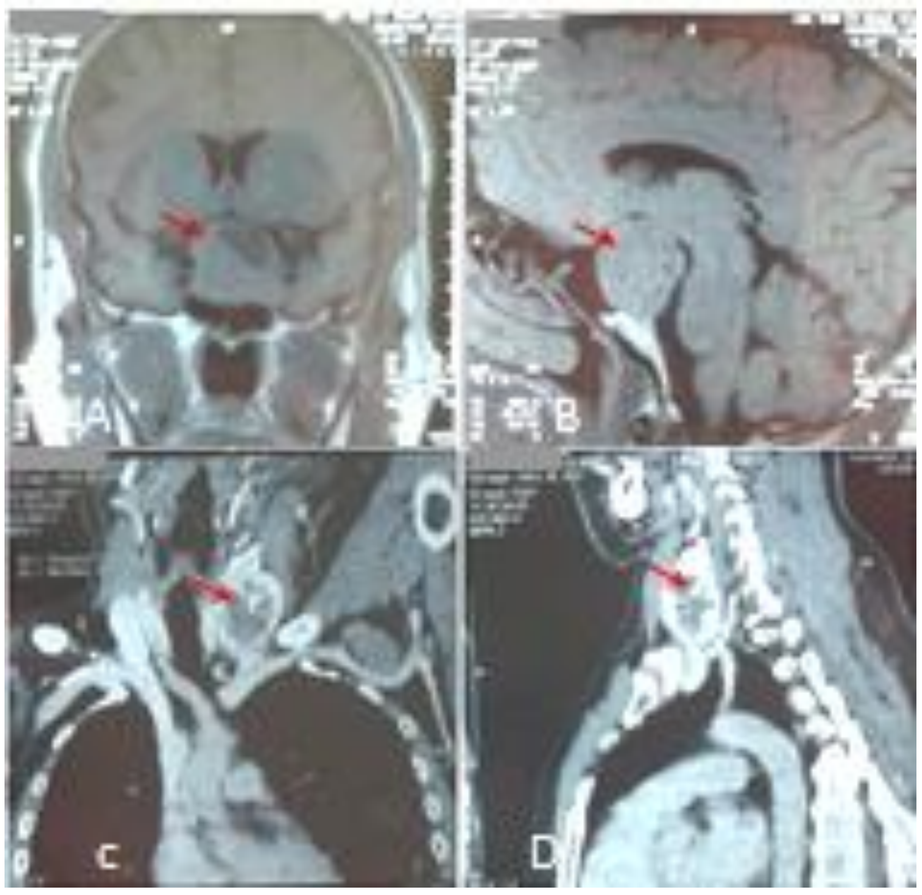

Fig.1: Association of pituitary Adenoma (A+B) and cervical Paraganglioma (C+D) in a 42 Years old patient.

CONCLUSION

In our series, PA in MEN1 and other endocrine neoplasia syndromes are common. Macro adenomas and secreting tumors are prevailing, with a variable aggressiveness. PA can be linked to one of four genes mutation (MEN 1, PRKAR1A, CDKN1B and SDH) that predispose to tumor formation. These syndromes should benefit from a genetic study for a rapid diagnosis and an early management of the affected patients and their families.

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