Introduction

Multiple endocrine neoplasia (MEN) are rare inherited disorders characterized by the combination of neoplasia or hyperplasia of two endocrine glands including MEN1: the association of pituitary, pancreatic and parathyroid tumors and MEN 2 regrouping NEM2a: medullary thyroid cancer (MTC), pheochromocytoma and parathyroid tumor and NEM2b with ganglioneuromas.

They're caused by autosomal dominant mutation: MEN1 gene (in MEN 1) and RET proto oncogen (in MEN 2).

Aim

Report the phenotypic and evolutionary characteristics of MEN.

Population and methodology

28 patients with MEN were hospitalized from 1981 to 2013. All patients received a guided exploration and molecular study for NEM 2.

Results: A preponderance of MEN2 (n:20, 71,42%) is observed.

In the 8 MEN1's cases, median age =41 years ±12,51 , first manifestation was pituitaty adenoma in 50%, following by hyperparathyroidism 37,5% and one case of cervical mass. 5 of them seem have a sporadic form and 3 had familial antecedent of MEN1.
The association hyperparathyroidism + pituitary adenoma was observed in 75% of the cases associated to: pancreatic (12,5%),adrenal tumor (25%), digestive carcinoid (12,5%), paraganglioma (25%).

The pituitary adenoma, diagnosed at age 37,67±13,37 was equally a prolactinoma (33,33%) or a non functional pituitary adenoma, a somatotrop (16,66%) and a gonadotrop adenoma (16,66%). A macro adenoma in 83,33 % (median height: 22,33 mm) treated surgically in half of cases and a medical treatment in all. Except one case of empty sella, others are still evolving.

Hyperparathyroidism was constant, discovered at age of 39,88 ±14,23 with a median parathormone's (PTH) rate of 487,25 ± 547,59 pg/ml caused by a unique adenoma (25%) or hyperplasia (12,5%) with a good post-operative evolution

In 20 MEN2 cases, we note 3 sporadic ones and 17 organised in 3 families, median age was 35,35 ±12,07, first manifestation: MTC(60%), phéochromocytoma (40%) revealed by cervical mass in 20%, high blood pressure 35% and a clinical screening 45%.

Tumors were bilateral in 57.84% of MTC, ¾ of pheochromocytomas and 33.33% of hyperparathyroidism.

MTC is constant, median tumor size in the is on average 29.24+/-17.99 mm rated (TNM 2007) stage I (70%), stage II (10%) and stage III (5%).

Hyperparathyroidism is found in half of cases, caused by parathyroid hyperplasia (20%) or adenoma (40%), management of others is ongoing. They benefit of a parathyroid resection with a good post operative evolution.

Pheochromocytoma were diagnosed at age 36 ±11,63 , with a median tumor size of 45,92±27,02mm, essentially >4cm and benefit in all cases of a surrenalectomy with two cases of controlateral recurrence.

The MEN2 phenotype was complete in 35%, partial in 65% with a good correlation genotype-phenotype in four families that express 634 mutation of RET gene and one case of 618 mutation.

We note a remission after management in only 35,7% of MEN1 patients and 40% of MEN2's.

Discussion:

Multiple endocrine neoplasia (MEN) are rare inherited multi glandular disorder characterized by an endocrine gland hyperplasia preceding adenoma and or cancer development.The expression of these diseases is extremely variable from a case to another and also in the same family. This variability results of a dissociation in time between the development of two affections. In agreement with literature MEN1 are rarer than MEN 2.Parathyroid hyperplasia, almost constant, is habitually the mode of revelation of MEN1.Often latent, it's symptomatic in only 10% (37,5% in our study).Unlike usual, first manifestation was represented in our series by pituitary adenoma. Pituitary tumors are habitually rarely revealing (10 %) of NEM I but in our series, it was the first manifestation in half cases. They are prolactinoma, somatotrop adenoma and more rarely non-secreting ones (unlike our patients that present equally prolactinoma or non-secreting adenoma in 33,33% followed by others). They are large, invasive and difficult to treat. Contrary to the literature where they are found in over 75 % of cases, pancreatic tumors are rare in our study (12,5%).Other rarer lesions (endocrine or not) have been described. Combination of clinical and genetic analyzes (unfortunately not performed in our patients, lack of reagents) has allowed many advances in the management of patients. Indeed, the genetic study permits an early mutation's identification in asymptomatic carriers, for whom regular clinical and laboratory monitoring is recommended.

MEN2 is more frequent. Its severity is related to the malignancy of thyroid tumors. These can be sporadic (60-655 % VS 48,71% in our series) or familial (30 % VS 51,28% our series). CMT occurs in almost all of MEN2 patients. The age of its onset varies depending on the type of mutation in RET gene. Genetic and family investigation allows doing an early and pre symptomatic diagnosis and then to treat effectively .All MEN2 patients don't develop systematically adrenal or parathyroid affection. The frequency of these diseases depends of the type of mutation of RET gene. They are most often benign. They must be regularly researched in case of genetic predisposition because of existence of a genotype phenotype correlation (observed in our patients). However, Unlike in MTC no preventive surgery is indicated.

Conclusion: MEN 1 and 2 are rare. We observed a preponderance of the MEN2. The molecular genetic testing should be extended to all of the MEN families to facilitate the management of these patients in a multidisciplinary approach.