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Multiple Endocrine Neoplasms Type 1 and 2 from Their Genetic Origin to the Clinic

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Abstract

Introduction: *Multiple endocrine neoplasms are a set of syndromes that are inherited in an autosomal dominant manner and are characterized by producing endocrine proliferative lesions, thus leading to hyperfunction of these glands. The characteristics of these lesions can be benign, malignant, or mixed.*

Methodology: *During this review, a search was carried out in different indexed journals and others, using keywords such as Multiple endocrine neoplasia, pheochromocytoma, Hyperparathyroidism, in order to obtain original and review articles whose publication had been carried out before 2020. were initially obtained articles but then applying our inclusion and exclusion criteria, we were left with 8 of which we collected the most applicable and relevant information possible.*

Results: *genetic alterations are undoubtedly the cause of the different types of MEN, in the specific case of MEN type 1, the gene present on the long arm of chromosome 11, band q13, is altered. In MEN type 2 the alteration is in the RET proto-oncogene, which in its normal form mediates the growth and multiplication of cells. The clinical manifestations of these pathologies will directly represent the neoplasm that is developing at that time with the greatest prevalence.*

Conclution: *It is important that in any isolated case of pituitary tumor, parathyroid tumor, medullary thyroid cancer, pheochromositoma or gastroduodenal pancreatic tumor, we study the possibility of some type of MEN. In the advanced stages of neoplasms, management is not very effective and very discouraging, for this reason the idea of screening relatives of those patients with MEN both type 1 and type 2 has been encouraged in order to be able to address them through a preventive management of neoplasms.*

Introduction

It was in 1968 when the term multiple endocrine neoplasia (MEN) began to be included in the medical field by Steiner et al1. He referred to this condition as a combination of endocrine tumors, where the main glands affected were the thyroid, the adrenal gland, and the parathyroid gland2. In addition to the lesions present on the endocrine system, non-endocrine lesions can also coexist, being direct consequences of chromosomal alteration of MEN.

Materials and Methods

A narrative review was carried out, in which the databases of PubMed, Scielo and ScienceDirect, Google Scholar, among others, were searched. The collection and selection of articles was carried out in journals indexed in English and Spanish. As keywords, the following terms were used in the databases according to the DeCS and MeSH methodology: Multiple endocrine neoplasia, pheochromocytoma, Hyperparathyroidism. In this review, approximately 22 original and review publications related to the subject studied were identified, of which 8 articles met the inclusion requirements required by us, which were full-text articles, which raised at least one of the aspects of the subject studied. Those articles that did not meet our requirements as a too old publication date, those that specifically spoke about the management of the pathology, were excluded.

Results

There are two categories of MEN:
° MEN type 1 or also called Wermer's syndrome which is rare yet has a high penetrance being an autosomal dominant pathology whose trigger gene was specifically located on the long arm of chromosome 11, band q13.3.
The main neoplasms that we can observe in MEN type 1 are tumors of the parathyroid glands in 100% of patients, the other alterations can vary in the percentage of appearance, such as pituitary tumors, reaching up to 60% of them. patients, tumors of the so-called gastroenteropancreatic system in up to 55% of patients. In addition, there are non-endocrine lesions that can arise as a manifestation of this type of MEN and they are facial angiofibromas which are skin lesions with characteristics similar to acne and that can appear in up to 88% of patients [4] followed by this non-endocrine manifestation there are other such as meningiomas, lipomas, ependimiomas, and leiomyomas.

To make the diagnosis of this entity, it would be thought that a range of molecular tests is required and the answer is yes, it would be the ideal in those cases in which investigative purposes are sought. But also the diagnosis can be carried out clinically without the need for genetic tests. This type of MEN can be diagnosed if we find in a patient at least two of the following endocrine lesions or also in patients who present only one type of tumor but have a first or second degree relative with an established diagnosis of MEN [5];
* Tumor of the parathyroid gland
* Pituitary tumor
* Tumor of the gastric, duodenal or pancreatic system (gastrinoma and insulinoma the most frequent).
° MEN type 2 or Sipple syndrome the appearance of this entity is conditioned by an alteration in the RET gene, which helps to control the way and speed with which cells multiply. An individual without any alteration inherits two copies of the RET gene, one from each parent, in those who develop the disease it may be because one of its copies is damaged and this could be due to an inheritance from one of their parents or a condition of this gene produced directly in the ovum or sperm, which would be a novice mutation and the child would be the first affected in his family, thus predisposing his offspring to suffer from the disease [6].

In the case of MEN2, there is a subclassification mediated by the organs they affect and the clinical expressions that it may or may not present;

MEN type 2A: this subtype of MEN2 tends to start in early adult life and presents with specific alterations such as Medullary Thyroid Cancer [TCM], Pheochromositoma and Hyperparathyroidism [7].

MEN type 2B: it is valid to suspect a type 2B multiple endocrine neoplasia in those patients in early childhood when they present TCM but also manifest the so-called mucous neuromas on the lips and tongue, they include an elongated face and protruding lips and their physical characteristics are those of a man with a tall and thin body [8].

Familial Medullary Thyroid Cancer [CTMF] is another variable in the presentation of MEN type 2, the diagnosis of this is carried out in those families in which 4 or more of its members manifest it but have absence of neoplastic lesions in other glands such as pheochromositoma or hyperparathyroidism.

Clinical Manifestations of Men Type 1 and 2

The signs and symptoms of the different multiple endocrine neoplasms are given according to the endocrine gandula they affect and the degree of compromise, which is why these manifestations are classified as follows:
1. Signs and symptoms of neoplasms in the parathyroid glands Altered mental status (tiredness, depression, confusion), weight loss, nausea, vomiting, constipation, increased urine output, dehydration, hypertension.
2. Signs and symptoms of neoplasms in the pituitary gland Gigantism, acromegaly, excessive growth of feet and hands.
3. Signs and symptoms of pheochromositoma High blood pressure, sudden severe headache, excessive sweating, fast heartbeat (tachycardia) and palpitations (interrupted heartbeat), feeling of extreme anxiety or fear, pain in the lower chest or upper abdomen, nausea with or without vomiting, weight loss, pale skin, feeling hot or intolerance to heat.
4. Signs and symptoms of Medullary Thyroid Cancer Lump or nodule in the front of the neck, hoarseness or difficulty speaking in a normal voice, cervical and supraclavicular lymphadenopathy, dysphagia, dyspnea.
5. Signs and symptoms of gastroduodenopancreatic tumors Pain in the abdomen, nausea and vomiting, loss of appetite, diarrhea, esophageal reflux, peptic ulcers [4, 5, 8].

Conclusion

MEN are an entity that, although rare, requires great clinical importance since its late diagnosis is associated with worse outcomes for patients. It is important that in any isolated case of pituitary tumor, parathyroid tumor, medullary thyroid cancer, pheochromositoma or gastroduodenal pancreatic tumor, we study the possibility of some type of MEN, in cases in which one of the multiple endocrine neoplasms of novice has already been diagnosed. it is important to screen the individual's family to make a timely diagnosis together with preventive or early treatment according to the case.

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