Tumeurs Neuroendocrines

Faiza Bereksi Reguig

Medical Oncology CHU of Sidi Bel Abbès, Algeria

Corresponding author: Faiza Bereksi Reguig, Medical Oncology CHU of Sidi Bel Abbès, Algeria. Tel: (+213) 792337287; E-mail: faizabereksireguig@yahoo.fr

Received: December 29, 2019, **Accepted:** January 08, 2020, **Published:** January 12, 2020

Keywords: Tumeurs, Neuroendocrines, Secretory, Chromogranin, Synaptophysin

Neuroendocrine tumors are tumors developed from cells of the diffuse endocrine system characterized by their secretory capacities [1]. These are tumors expressing endocrine (chromogranin) & neuroendocrine (Synaptophysin, NSE) markers. These tumors are rare; the annual incidence of this disease is estimated to be 2 to 5 new cases per 100,000 inhabitants, based on data from different sources, the incidence and prevalence of NETs are increasing compared to that of all malignant neoplasias [2-4]. The age of onset is most often between 40 & 60 years old.

The TNE Characteristics; these are rare tumors, often slow-growing, with a less severe prognosis compared to other cancers; they have the ability to secrete peptides, hormones; We will then speak of a “functional” tumor [1,2]. These hormones are of different types: most often, it is serotonin, more rarely insulin, gastrin, or glucagon. These hormonal secretions will cause manifestations different clinics, which may be at the origin of their discovery.

They can be localized throughout the whole organism Their location, the most frequent are digestive in 60% of cases, especially the small intestine, the appendix, the stomach, the rectum, the pancreas, sometimes the lung,

but it can be found in all organs: colon, skin, kidneys, larynx, esophagus, ovaries and bladder [2,5,6]. They are sporadic in the majority of cases, diagnosed without any cause or contributing factor being identified [7]. However, certain tumors ($\leq 5\%$ of total NETs) are of genetic origin and arise in the context of hereditary syndromes predisposing to tumors, called: multiple endocrine neoplasia type 1 (NEM1), Von HippelLindau disease, Bourneville tuberous sclerosis and type 1 neurofibromatosis.

The circumstances of discovery of NETs are very variable. They can be present for several years without causing the slightest problem & are diverse and depend in particular on the functional character (secreting) or not of the tumor. Four types of clinical presentation can lead to suspect an endocrine tumor.

Symptoms suggestive of a tumor syndrome the clinical signs essentially depend on the location and type of tumor. It can be intestinal manifestations (occlusion), abdominal pain, bleeding in the stool, perception of a mass in the abdomen or respiratory infections or bronchial bleeding. These signs are not very specific because they can exist in very many other ailments, notably mild. Sometimes it's fever, weight loss or lack of appetite,

or the discovery of metastases.

Symptoms related to the hormonal tumor secretion responsible for the discovery in less than 20% of cases. Depending on the type of tumor, the hormones produced will be different, leading to various clinical signs. One can have diarrhea, abdominal cramps, episodes of skin flush, breathing difficulties evoking asthma, signs of hypoglycemia, recurrent ulcers, heartburn, reflux, diabetes.

Lucky find. During an imaging examination (standard radiography, scanner, ultrasound), during surgery (appendicitis), or during endoscopy (gastroscopy, colonoscopy). A screening; during an assessment of a genetic disease predisposing to NETs.

The diagnosis of neuroendocrine tumor is often established by analysis of the operating room or during a biopsy. The pathologist confirms the neuroendocrine tumor on its appearance under the microscope and on the existence of specific markers such as chromogranin A or synaptophysin; it also specifies tumor differentiation [8,9]. A distinction is made between well-differentiated tumors (these are often secreting tumors) and poorly differentiated tumors [8].

The additional assessment which will be made according to the location of the tumor and its clinical and biological presentation. The purpose of this assessment is to specify the characteristics of the tumor and the type of hormonal secretions, the tumor extension and to detect hereditary cases. It is based in addition to the pathology examination, on biological examinations and imaging. The biological assessment measures the production of certain markers in the blood, in particular chromogranin A [9]. Other markers may be measured in the blood and urine depending on the symptoms experienced by the patient, in particular the 5-Hydroxy Indol Acetic Acid (5-HIAA) (10) in 24-hour urine, which reflects secretion of serotonin by tumor.

The aim of imaging examinations is to find the initial site of the tumor, to carry out an extension assessment and then to follow the progression of the tumor. They consist of conventional imaging exams (ultrasound, scanner, MRI) and endoscopic exams. There are also more specific examinations: metabolic imaging exams such as somatostatin receptor scintigraphy (SRS) also

called Octreoscan®, it provides details on the primary tumor and participates in the extension assessment. It is especially requested in the event of a well differentiated NET or PET-FDG, Tomography by positron emission with 18-FDG (TEP-FDG) (also called PetScan). Done after the injection of a radioactive glucose-based product, it is performed, in addition to the previous examinations, especially in cases of poorly differentiated NET or rare cases of well-differentiated tumors. In particular, it allows an assessment of the spread of the disease.

The prognosis of NETs is variable and will depend on many factors: The degree of differentiation of tumor cells; The site of the primary cancer, its size, the localized or spread to other organs, the existence of metastases and finally on the existence of possible hormonal secretion. Therapeutically; taking into account the great diversity of NETs and their great heterogeneity in their evolutionary profile, the therapeutic management is complex and must be adapted to each patient. This must be done by a multidisciplinary specialized team (RCP), associating the required doctors but also, the geneticist and the biologist.

The treatments have a double objective: to remove the tumor and to control the hormonal secretions. These treatments can be prescribed alone but they are most often combined and adapted to the profile of each patient.

1. Simple monitoring without treatment may be offered during initial care or after one or more treatment sequences. This attitude is justified by the progressive slowness of certain tumors, the toxicity of certain treatments but also the need for a recovery period for the organism. This “active” surveillance strategy should not be interpreted as an absence of a therapeutic solution.

2. Surgery is the most effective way to cure neuroendocrine tumors when they are localized. It consists of the removal of the tumor, especially when it sits in the rectum, lung, pancreas, appendix or duodenum. Some small, accessible stomach, duodenum and rectum tumors can be removed endoscopically. Surgery is also offered on a case-by-case basis to treat local and / or metastatic relapses.

3. Medical treatment: Anti secretory treatments; whose main objective is to decrease the hormonal secretions

of the tumor, which are often responsible for many symptoms. Sometimes a direct effect by stabilizing tumor progression. It is often the first treatment prescribed, before surgery. The most commonly used drug is a somatostatin analog [11,12]. This substance will bind to tumor cells and thus block or reduce the production of hormones by the tumor.

Two drugs can be prescribed: Sandostatin® (octreotide), prescribed as a daily subcutaneous or intramuscular injection, and Somatuline® (lanreotide) administered by monthly subcutaneous injection [11,12]. These treatments are generally well tolerated. Sometimes there are some transient digestive side effects at the start of treatment such as nausea, diarrhea, bloating or abdominal cramps.

Other more specific antisecretory treatments are also used depending on the type of tumor and the hormones produced, such as PPIs in gastrinoma or diazoxide (Proglycem®) in insulinoma. When the response is favorable and the treatment is well supported, it can be continued for several years.

Chemotherapy is a medical treatment that aims to slow or even stop the growth of cancer cells. This is a general treatment, taken orally or injected into the blood. It is useful in certain NETs, at the stages of metastases. Several products are used which are often associated with each other. The indication for chemotherapy but also its modalities depend on the differentiation of the tumor and its initial location. The total duration of chemotherapy is variable depending on its effectiveness and the side effects experienced by the patient.

External radiotherapy, the objective of which is to destroy diseased cells by ionizing radiation. Radiation therapy is used in some tumors, sometimes in combination with chemotherapy.

Metabolic radiation therapy (RTM), or “internal radiation therapy”, is a method of specifically irradiating cancer cells scattered throughout the body. This treatment consists in fixing a radioactive molecule (radionuclide) on a somatostatin analog, which will thus lead the radioactive product to the tumor. Several radionuclides can be used: Yttrium 90, Lutetium 177 or Indium 111.

Metabolic radiation therapy (RTM), or “internal radiation therapy”, is a method of specifically irradiating cancer cells scattered throughout the body.

This treatment consists in fixing a radioactive molecule (radionuclide) on a somatostatin analog, which will thus lead the radioactive product to the tumor. Several radionuclides can be used: Yttrium 90, Lutetium 177 or Indium 111.

At the end of the treatment, very regular monitoring will be carried out for several years. The rhythm of this monitoring must be established individually by the doctor in agreement with each patient.

Regular long-term monitoring is essential. She also assesses the effectiveness and side effects of the treatments. It is based on interrogation, biological examinations (hormonal assays, etc.) and imagery (scanner, MRI, scintigraphy, etc.) which make it possible to assess the course of the disease and to look for a possible recurrence of the tumor. Indeed, any relapse of the disease must be managed and appropriate treatment started.

Conclusion

The treatment of patients with neuroendocrine tumors must take into account a standardized characterization in accordance with the guidelines, while integrating prognostic diversity. Controlling hormone-related symptoms is essential with Optimizing the long-term benefit-risk ratio. New treatment options and urgent trials are more than necessary.

Reference

1. Vinik AI, Woltering EA, Warner RR, Caplin M, O'Dorisio TM, et al. (2010) Nanets consensus guidelines for the diagnosis of neuroendocrine tumor Pancreas 39: 713-734.
2. Klimstra DS, Modlin IR, Coppala D, Lloyd RV, Suster S. et al. (2010) The pathologic classification of neuroendocrine tumors: a review of nomenclature, grading, and staging systems Pancreas 39: 707-712.
3. SEER data between 1973-2004.
4. Yao JC, Hassan M, Phan A, Dagohoy C, Leary C, et al. (2008) One hundred years after “carcinoid”: epidemiology of and prognostic factors for neuroendocrine tumors in 35,825 cases in the United States J Clin Oncol 26: 3063-3072.
5. Frilling, Akerström G, Falconi M, Pavel M, Ramos J, et al. (2012) Neuroendocrine tumor disease: an evolving landscape. Endoc Relat Cancer 19: R163-85.

6. Modlin, Oberg K, Chung DC, Jensen RT, DE Herder WW, et al. (2008) Gastroenteropancreatic neuroendocrine tumours. *Lancet Oncol* 9: 61-72,
7. National Comprehensive Cancer Network®. NCCN Guidelines® for Neuroendocrine Tumors v 2.2014 sporadic.
8. Öberg K (2010) Pancreatic endocrine tumors. *Pancreatic endocrine tumors Semin Oncol* 37: 594-618.
9. Vinik AI, Woltering EA, Warner RR, Caplin M, O'Dorisio TM, et al. (2010) Nanets consensus guidelines for the diagnosis of neuroendocrine tumor *Pancreas* 39: 713-734.
10. Jensen RT, Cadiot G, Brandi ML, DE Herder WW, Kaltsas G, et al. (2012) Enets Consensus Guidelines for the management of patients with digestive neuroendocrine neoplasms: functional pancreatic endocrine tumor syndromes *Neuroendocrinology* 95: 98-119.
11. Rinke A, Müller HH, Schade-Brittinger C, Klose KJ, Barth P, et al. (2009) J Clin Oncol Placebo-controlled, double-blind, prospective, randomized study on the effect of octreotide LAR in the control of tumor growth in patients with metastatic neuroendocrine midgut tumors: a report from the PROMID Study Group 27: 4656-63.
12. Phan A, Kunz PL, Reidy-Lagunes D, Anthony LB, Bertino EM, et al. (2013) Consensus guidelines for the management and treatment of neuroendocrine tumors. *Pancreas* 42: 557-77.

Copyright: ©2020 Faiza Bereksi Reguig. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.