

Approximation to the Patient with Tumor of Unknown Origin

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Abstract

The tumor of unknown origin constitutes 3-7% of the cancers studied and is one of the 10 most frequent cancer diagnoses. It is a malignant tumor whose first origin or identification is not done in the clinical history, in the clinical exploration or in the complementary studies. At present, the effort in the primary search for the origin of the cancer that will be directed at specifying these entities and recognizing them as soon as possible is arduous. Today we have several techniques among which we highlight immunohistochemistry, molecular biology and radiodiagnosis that greatly facilitate the work of the clinician in detecting the origin of tumors, although none of them is conclusive.

Keywords: Cancer of unknown origin; Tumor; Diagnosis; Treatment

Introduction

According to epidemiological data, carcinoma of unknown origin accounts for 2.3-4.2% of all human cancers and is one of the 10 most frequent cancer diagnoses [1]. The most important thing is to discover within the patient group the most effective treatment for the exhaustive search of the primary tumor. At present, different maneuvers are being carried out for detection, such as anamnesis that seeks the physical and psychological examination of the patient to find the source of the tumor, the physical examination that must be complete and well performed by the physician, and the complementary tests, mainly Laboratory and imaging tests [2].

The next important step is to remove the sample from the affected tissue. The biopsy is possibly the most important test for the early diagnosis of the tumor of unknown origin. Another widely used test is needle aspiration with a fine needle, this is a quick and very simple test that can provide great information to the doctor about the origin of the cancer.

The anatomopathological study of the sample is probably the most important because it will help to find the origin of the cancer. These tests consist of looking under the microscope for the tissue sample. This implies that the researcher must be very familiar with the tissues in order to be able to find the cancerous cells. In addition to the optical microscope, there are other imaging techniques such as electron microscopy or cytogenetic studies.

If these tests are not performed correctly, a diagnosis can not be made and the prognosis of the patients becomes very poor, with an average survival of 3-4 months, only 25% of patients are alive per year and 10% at 5 years old.

With these data so discouraging researchers must determine how much diagnostic effort is necessary before accepting a diagnosis of tumor and also consider whether a more accurate diagnosis will have an impact on the type of treatment to be applied and the overall survival of the patient [3].

Diagnosis

As we have discussed in the introduction, the early diagnosis is the most important thing to determine the origin of a tumor. The diagnosis will be directed at recognizing the subgroup of patients within the heterogeneous group of cancer of unknown origin in order to diagnose and use a specific treatment for this patient, which improves survival.

Anamnesis and clinical history

It is essential to make a complete and correct medical history. To do this, we must follow the normal steps of a complete anamnesis knowing the habits of the patient as well as the environmental influence in which he lives. It is also important to emphasize the results of previous biopsies, surgeries and resected lesions, if we had them, as well as in the family history of oncology that may determine a family predisposition to some types of tumors such as colon or breast among others [4].

Physical examination

The physical examination is probably the most important part in the early detection of a malignant tumor. It should first include a thyroid, mammary, lymph node, prostate, gynecological and rectal palpation to evaluate the most common tumors in patients. Malpractice or performing physical examination quickly and incorrectly can reduce early tumor evaluation by 50%. Thus, correct and slow palpation is recommended to evaluate all structures [5].

A mass is an abnormal area, such as an inflammation or firm area that can be caused by a tumor. This can be caused by the growth of cancer in the liver or, less frequently, in the spleen. It should also be noted that the difficulty in breathing may be the result of a cancer that has spread to the lungs or the accumulation of fluid and cancer cells in the area around the lungs

The visualization of the patient is also important. Some types of cancer that are generated in the internal organs can spread through the bloodstream and reach the skin. Since it is very easy to see the lumps

on the skin, the metastases in the skin are sometimes the first sign that a cancer of unknown primary origin has spread [6].

Serological tumor markers

Tumor markers are not new to medical practice if one considers that their history dates back to the mid-nineteenth century, when Henry Bence-Jones reported the precipitation of a protein in the acidified urine of a patient with multiple myeloma [7], Describing the first tumor marker [8-9], which is known by its name: Bence-Jones protein, still valid in clinical practice.

Although there is no ideal tumor marker, as has been clearly explained, in the world medical literature there is sufficient support for the use of tumor markers in the different stages of the medical act [8,9]. According to international laboratory standards, a test can be used in five clinical scenarios: as a screening test, as a diagnostic test, including the actual diagnosis, differential diagnosis and prognosis, as a predictive test, as a test to follow And evaluate the outcome of the treatment, and as a test to detect relapses, as will be discussed in detail in the following subheadings [10].

Image studies

Imaging studies use sound waves, X-rays, magnetic fields, or radioactive substances to get pictures of the inside of the body. Imaging studies can be done for a number of reasons, including a closer look at an abnormal area that may be cancer, how far the cancer may have spread, trying to determine the origin of the cancer, and help determine if the cancer Treatment has been effective.

Endoscopic procedures: Endoscopic procedures allow a direct view of the tumor, obtaining tissue samples and excision in cases of small tumors. Procedures that may be useful in the diagnostic investigation of tumors include upper gastrointestinal endoscopy (for gastric and duodenal tumors), endoscopic capsule (for intestinal tumors), and colonoscopy (for tumors of the rectum and colon). Bronchoscopy and thoracoscopy are indicated in the identification of bronchopulmonary tumors, whereas mediastinoscopy can be used in the study of mediastinal masses [11].

Transabdominal ultrasound: Transabdominal ultrasound can identify up to one-third of intestinal carcinoids and two-thirds of liver metastases. It may also serve as a guide for transcutaneous liver biopsy. The sensitivity of this technique in the diagnosis of tumors is variable (between 20 and 86%) and depends largely on tumor size. The drawback of this procedure is that tumors on the surface of the pancreas or in the duodenum are barely visible [12].

Radiological techniques: The simple chest X-ray has utility in the detection of bronchial carcinoid tumors, pulmonary metastases and thymic masses. Studies of the esophagus, stomach and duodenum as well as intestinal transit and opaque enema can be used for the detection of tumors of the digestive tract. Enteroclysis is a technique that uses barium contrast and can be combined with images obtained in tomographic techniques. Computed tomography and magnetic resonance imaging are the most widely used imaging tests for cancer diagnosis [13].

Magnetic resonance: This test can be used to confirm a finding of tumors or to locate an injury that has not been demonstrated in other tests. The appearance of the tumors is that of lesions of low signal intensity in T1 and high in T2. Fat saturation increases the visibility of

the lesions. Injection of gadolinium also improves the image due to the vascular component of the tumor. The sensitivity of modern magnetic resonance imaging techniques in tumors is similar to that of tomography and ranges from 91 to 94%.

Anatomopathological tests analysis

Links that contain schematic explanations of many of the techniques are included in the appendix.

Histopathology: It comprises the macro and microscopic evaluation of the tumor tissue. It reports the presence of tumor, margins, neurological origin or not, histological classification and degree. Tumor heterogeneity forces multiple fragments to be studied. Intraoperative information should be included to aid in the surgical decision.

Immunohistochemistry: It is essential in the pathological diagnosis. It is based on the recognition of tissue antigens by specific antibodies. It has progressed enormously with the development of high specificity monoclonal antibodies [14,15].

Molecular genetic: It values genetic alterations at the molecular level. These techniques are allowing us to delve into the pathogenetic mechanisms of cancer, both in the alterations that occur in genes related to oncogenesis [16].

Treatment Recommendations

We can divide the patients into two groups, one that has a tumor location or metastasis, and another group that knows patients with several affected areas.

Patients with a single metastatic location

Local treatment with surgery and/or radiotherapy should be performed. The role of "adjuvant" systemic chemotherapy is unknown. It constitutes 5% of the cases of tumor of unknown origin. They are usually middle-aged or advanced patients with a history of smoking and alcohol consumption. In most cases, metastases are located in the cervical or supraclavicular lymph nodes and less frequently in inguinal lymph nodes or other locations.

Patients with involvement in other different areas

It usually corresponds to metastasis of occult lung carcinoma. The tests that must be performed for the diagnosis are mainly a thoracic and a fiberoptic bronchoscopy. In the presence of clinical features that do not suggest lung cancer, consideration should be given to the possibility of squamous metaplasia in undifferentiated carcinomas and to insist on immunohistochemical evaluations (Table 1).

Treatment in almost all cases is palliative in almost all cases. If the patient's situation allows it, chemotherapy regimens, usually based on platinum, may be used. Malignant neoplasm, poorly differentiated carcinoma or adenocarcinoma, it accounts for 35% of cancer cases, unfortunately being younger patients with rapid tumor growth.

Metastases are located predominantly in peripheral, mediastinal and retroperitoneal lymph nodes. The clinical and pathological evaluation should be extremely careful because in this group are neoplasias highly sensitive to chemotherapy and potentially curable with appropriate treatment.

Histology	Adenocarcinoma	Squamous cell carcinoma	Carcinoma or Adenocarcinoma
Armpits	Adenopathies in armpits, carcinomatosis, bony metastases	Cervical adenopathy, inguinal adenopathy	High or low grade neuroendocrine tumor.
Treatment	Follow the same procedure used for breast, ovarian, prostate or radiotherapy	Follow treatment for neck cancer or lymphadenectomy with or without radiotherapy	Continue as the cases of advanced carcinoma, platinum plus ectopic or with taxane.

Table 1: Recommendations for the treatment of different tumors.

Future Perspectives

Molecular biology techniques must be incorporated into the routine histopathological and immunohistochemical diagnosis of tumors that have an unknown origin to find out more about their development. At the moment, at least, the study of this type of cancer is essential.

It is necessary to employ simple and standardized methods. This requires the adoption of universal validation criteria. In addition, techniques are being developed to study in peripheral blood these genetic markers that may help in the future to its diagnosis.

In research, large-scale studies are being carried out using new technologies such as microarrays that allow in-depth analysis of pathogenic pathways, new molecular markers, RNA expression profiles or the development of new therapeutic strategies based on the molecular biology of cancer.

The need for multicentric studies to help the elimination of cades from the earliest stages should be emphasized.

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