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SUMMARY

Frequency measures of this pathology play an important role in any epidemiological explanation; however, they can be confused with similar situations, which is why it is important to start by defining them correctly. Prevalence measures describe the proportion of the population suffering from the pathology under analysis at a given time; these patients may be new cases or survivors of the pathology. Incidence measures, however, refer only to the number of new cases that appear within a defined period of time. Prevalence is of course dependent on incidence, as well as on the duration of oncological diseases, changes in recovery, or patient life expectancy.

Keywords: oncology, oncology clinic, cancer research, tumors, oncological surgery

CHAPTER: 1

CARCINOGENESIS, ASPECTOS MOLECULARES.

Pathology frequency measures play an important role in any epidemiological explanation; However, they come to be confused as similar situations, so it is essential to start by defining them correctly.

Prevalence measures describe the proportion of the population suffering from the pathology analysed at a given time; these patients have the possibility of being new or survivors of the pathology. Incidence measures, however, refer only to the number of new cases appearing in a given time. Prevalence is of course dependent on incidence, but in addition to the duration of pathology, by changes in recovery or life expectancy of patients.

Carcinogenesis

Carcinogenesis is the process by which traditional cells become malignant cells. Our organism is made up of 100 billion differentiated cells that fulfill specific functions and, to distinguish the cells of the central nervous system (CNS), undergo cell separation controlled by a stimulatory system and another inhibitory, which are commanded by 23 chromosomes inherited from the mother and 23 from the father.

The genetic material is arranged in 4 bases -adenine, thymine, guanine and cytosine- which, like steps of a ladder, remain supported on a phosphorylated pentose, deoxyribose, forming a nucleic acid called DNA (deoxyribonucleic acid). When there are 2 strands of DNA rolled up on themselves, adenine is coupled to thymine and guanine to cytosine, forming such true base pairs.

There are primordial proteins called histones that participate in the organization (packaging) and functionality (transcription of the genetic code) within the nucleus.

Each cell, in its 46 chromosomes, hosts between 30,000 and 40,000 genes, which have a variable number of base pairs, ranging from thousands to millions. Hence, certain genes are longer than others, just like chromosomes.

Each gene has sectors (exons) regulating the transcription of code from the gene to the cytoplasm

for the synthesis of structural or enzymatic proteins, and that transcription is accomplished by means of RNA (ribonucleic acid), where sucrose deoxyribose is replaced by ribose and thiamine base by uracil. This messenger RNA makes the transduction of the message from the nucleus to the ribosome located as an organelle inside the cell cytoplasm, and there it "manufactures" the protein that will fulfill specific functions inside and outside the cell. In addition, there are non-coding DNA regions called introns.

Microsatellites are short fragments of cyclic DNA found in all chromosomes. The number of microsatellites has been linked to the area of carcinogenesis, as they generate some instability in the genome. In the human species there are genes «repressed» (because they «go silent» during embryogenesis and organogenesis) by epigenetic effects.

Those «repressed genes» have the possibility of being activated again and the cell return to its all-potential state. Depression belongs to the biological mechanisms that can be fulfilled in a cancer cell, and this cell become undifferentiated, free to all regulatory mechanisms and immortal. These facts argue that, once cancer is created, certain antigens which are only expressed in primitive cells have the possibility to express themselves again and serve as tumor markers.

Cell duplication is done by means of the normal cycle of the cell, which consists of the following stages:

- Stage G0: the cell is in a quiescent state.
- Stage G1 (GAP = interval): the cell pairs the resources needed for duplication of genetic material (9 h).
- Stage S: in this stage the duplication of the genetic material is fulfilled (10 h).
- Stage G2: the cell is processed for mitosis (there are already 2 chromatids) (4.5 h).
- Stage M: mitosis (mother cell gives rise to 2 daughter cells) and cytokinesis (physical separation of the cytoplasm in 2 daughter cells at the extent of cell separation). Loss of control points leads to the development of cancer (point G1 in transition G1-S; point G2 in the transition G2-M).

Risk factors in cancer development

Danger element linked to greater possibility of a person developing a pathology or other health problem. Cohort analysis is the best way to identify hazard components, as it is observational and prospective. People are evaluated on the functionality of the existence or absence of exposure to a defined element of danger. Initially, all competing elements remain free of the pathology of interest and are continuous over time; if, at the end of this observation period, the incidence of pathology is greater in all those exposed to the hazard element, it is concluded that there is a grouping between exposure to the variable and the incidence of pathology.

Carcinogens in the environment

Carcinogen is one whose management leads to an increase in the incidence of malignant neoplasms. The etiology of cancer remains undefined; however, notable evidence indicates the predominance of environmental and lifestyle components, which was seen from the 16th century onwards: Von Hohenheim (1700) associated mining with lung cancer, possibly by radon gas; Hill (1761) associated tobacco with nasal cancer; and P.Gramo. Unna (1894) associated exposure to sunlight with skin cancer.

Damage to DNA and cancer

Damage to DNA by various components leads to compensation mechanisms. In 1980, P. C. Hanawalt was one of the first to disseminate mechanisms of UV-induced DNA damage in human fibroblasts.

We now understand that there are mechanisms which repair DNA malady, such as the NER (nucleotide cleavage repair), BER (base cleavage repair) and MMR (base malpairing repair) pathways, which work in a balanced way, so in the absence of one, Someone else replaces him.

The reaction of the cell to damaged DNA by means of such healing systems is a complex process of several steps that includes well over 20 proteins. A defect in any of them confers deficiencies in their composure.

Hereditary cancer

Although cancer is considered an acquired disease, there is evidence that hereditary components also play a role. These neoplasms are caused by mutations in tumor suppressor genes affecting one of the alleles of a mutated gene, implying that a point mutation in the other allele causes the appearance of the tumour cell and then the carcinoma.

Immune system, inflammation and cancer

Regulatory T cells are relevant in cellular homeostasis, because they exert suppressive effects against infections, by cell-to-cell contact or release of interleukin (IL) 2, IL-10, β transformant enhancement component, IL-35 and activation of the PD1 pathway.

Neutrophils are considered the first line of custody throughout infections and inflammation, exerting their action through phagocytosis and antimicrobial enzymes; However, they are also found in the microenvironment of different neoplasms as a result of chemokines that attract them. According to the evidence available at that time, its presence is associated with a poor prognosis.

Idiopathic inflammatory bowel diseases (Crohn's disease, 2.5% risk; chronic ulcerative colitis, danger of 3.7%) predispose to risk of developing colorectal cancer 8-10 years later than the diagnosis.

Anti-proliferation signals: the adaptability of the tumour cell

The cell cycle, is known as a regulated process in the cell that generates separation into 2 daughter cells. The loss of control in the mechanism of cell proliferation signaling pathways causes malignant cells to generate a greater proliferative capacity and evasion to the immune system.

Anti-proliferative signals inhibit the growth of normal cells; However, when tumour suppressor genes are inactivated, mechanisms that block cell growth are altered, such as cell quiescence by G0, where the cell leaves the cell period and stops its growth, and induction into the post-mitotic state.

Most of the anti-proliferative signals are regulated by 2 tumor suppressor proteins, Rb and p53, which play a central role in designating whether cells proliferate or gain senescence or apoptosis. It was shown that 70% of firm tumors show alterations in tumor suppressor genes.

Retinoblastoma: the primordial guardian of the genome

The function of the tumor suppressor protein retinoblastoma (Rb) is to restrict passage from the G1 stage to the S stage of the cell period.

The Rb protein interacts with members of the E2F transcription element. The relationship in the middle of proteins

Rb and E2F blocks the trans-activating functionality of E2F and stops cells from accessing the S stage. Throughout the G1 cell period stage, the Rb protein is in its hypophosphorylated form, which prevents the production of cyclins and CDK by binding to the E2F protein.

Once the cells are stimulated to proliferate by external signals in their microenvironment, G1-specific CDKs accumulate and phosphorylate on the Rb protein, causing E2F to be released and continuing this cycle. Dephosphorylation of the Rb protein causes the cell to senescence.

Avoidance of apoptosis: a primary mechanism in the malignification process

Apoptosis is a genetically programmed cell death process for the suppression of cells that have an irreparable variation or dysfunction; it has been shown that it can also be induced in various human pathologies.

The cellular process begins with a cellular condensation and the formation of vesicles that are to be phagocyted and digested by neighboring cells. Two pathways of apoptosis induction are known: the mitochondrial pathway, called intrinsic pathway, and the death receptor-induced pathway, called extrinsic pathway. The analysis of apoptosis is well over 40 years old, it was born as an analysis of why spontaneously in tumors is shown and exacerbated with radiotherapy or chemotherapy treatments. Another observation was given by the resistance to apoptosis in malignant cells.

Angiogenesis: grow or not grow

Angiogenesis is the biological process by which new blood vessels are created and grown from pre-existing blood vessels. It is a fundamental and important mechanism in embryonic development, tissue regeneration and wound healing.

Tumor angiogenesis is a process in which the formation of intratumoral blood vessels from the same tumor cells is induced, promoting the formation of new blood vessels in the tumor for its development and growth. This process is called vasculogenic mimicry.

Angiogenesis is also activated by tissue hypoxia to maintain proper oxygenation. Once a tissue undergoes hypoxia, mechanisms that induce the expression of pro-angiogenic proteins are activated.

In the first activated components are the hypoxia-induced components (HIFs), which activate the expression of pro-angiogenic genes. The premise of angiogenesis-dependent tumor growth is conceptually the observation that it is elementary, but not sufficient, to advance tumor growth, and although lack of angiogenesis may delimit tumor growth, angiogenesis in a tumor enables, more does not ensure, tumor increase.

Proliferation: the limitless replicative potential in cancer

In organisms, cells are in a quiescent state and only several specialized cells such as hematopoietic or epithelial cells maintain their proliferative activity. For that, the cell executes a sequence of biomolecular processes called in general cellular period, which is supported on 4 stages: G1, S, G2 and M. The transition from one stage to another in the cellular period is regulated by different proteins, CDK, cyclins and positive regulating proteins (protooncogenes) or negatively (tumor suppressor genes).

To protect the entirety of chromosomes finally from the cell period, the cell has a composition at each end of the successful chromosomes as telomere, which, together with telomerase and several chaperone proteins, serves as a protective hood to defend against the degradation of genetic material after each replication period is completed. Sporadic or inherited mutations in the genes involved in these surveillance pathways contribute to an increased risk of cancer development.

Although in certain types of cancers, telomerase overregulation occurs at early stages. Introduction of hTERT before or between senescence and cell crisis results in direct immortalization. The ability of cells to stop the cell period after suffering a DNA malady is crucial once genes are altered, cells proliferate uncontrollably and cancer is created. Currently there are investigations for drugs

anticancer, the prime candidates for such tactics.

Metastasis: the aberrant pathway of clonal extension

At the beginning of the cascade of metastases, angiogenesis allows the extension of the primary tumor and grants a growth in the area of vascular area that enables the tumor to escape into the circulation and extension of metastatic implants.

Most of the tumors are born without angiogenic activity, there is in situ stage without neovascularization for long periods. Neovascularization begins once a subgroup of cells within the tumor changes to an angiogenic phenotype. In some cases, this change may occur prior to the tumor being fully developed (preneoplastic or preinvading stages).

In the end, the explanation and reasoning of the cellular processes usual in all types of cancer called "cancer seals" represent an immeasurable source of modalities and possibilities, where the investigation has laid the molecular bases of these processes, which have served as a platform for the development of novel cancer procedure tactics leading to personalized and accurate medicine, where by silencing or inhibiting certain molecules we can collapse or maintain the control of complicated pathologies such as cancer, generating fewer side effects that impact on the quality of life of patients.

CHAPTER: 2

STATIONING AND PRINCIPLES OF TREATMENT.

Malignant neoplasms are characterized by disordered cell growth, have the possibility of forming masses or tumors in the place where they originate, and have the function of bursting neighboring tissues and developing locoregional and distant increase.

The expansion of the pathology at the moment of diagnosis is fundamental because it helps to establish the state of the pathology, the ideal therapeutic project and, most importantly, establishes the prognosis of the pathology. It is universally known that tumors confined to the place in which they originated have a better chance of cure or better universal evolution than those that show expansion of the tumor to neighboring tissues or distance.

It is a categorization based on anatomical expansion properties.

The specification of «T» derives from the properties of the primary tumor, and in most neoplasms is a parameter in millimeters or cm (breast, melanoma, cervicouterino), but in several other neoplasms will be determined by expansion into the layers of the epithelium or expansion to surrounding tissues (digestive tract, skin, endometrium, vulva, bile duct). The explanation of «N», which is derived from the nodal English word, refers to the lymph nodes or the carrying lymphatic area related to the tumor zone. And referring to the explanation of «M», taken from the word metastasis, and as its name suggests, will describe the existence or not of distal tumor activity.

In general terms, these 3 morphological limits of the tumor are grouped, validated in monumental patient series and based on algorithms give us information that translates into homogeneous sets of patients (stages), and all of them shows prognostic differences in pathology.

These phases, by providing prognostic information, help us to establish the procedure that would best benefit the patient. For example, it would help us to choose whether to operate on a patient in a primary way or to submit him to chemotherapy with neoadjuvant objectives.

This categorization is the universal standard for oncological pathologies, although it can be said that over time other prognostic components besides those of TNM have been found with great relevance in prognosis, such as tumor markers and biological profiles, which have helped to conceptualise more

specific treatments. The TNM categorization shows different nomenclatures in relation to the manner and timing of assessment, whether pre-surgical or post-procedure clinical assessment, or if the lesion to be assessed is secondary to a tumour recurrence.

The TNM information has to be entered in the file at the time of the step-up. Once it is based on macroscopic boundaries, that is, on the initial clinical data with which the patient is received at the consultation, without having undergone any previous procedure (purely clinical classification), it is assigned as a prefix the letter «c» (cT, cN, cM), and for its evaluation we use, in addition to the clinical study, endoscopic or imaging studies that give us an approximate measure of the tumor injury or expansion.

If the patient is submitted to surgical resection in an initial manner and the original tumor findings remain based on histopathological reports, the prefix «p» (pT, pN, pM) is written for its entry, and usually this specification is more accurate in relation to clinical findings.

Another variable in this categorization is once the expansion of the pathology is documented subsequent to receiving any type of oncological procedure regularly with the aim of minimizing the magnitude or expansion of the pathology, as chemotherapy, radiation therapy or immunotherapy - treatments called neoadjuvants.

Once the lesion is explained, the letter «y» is applied and followed by «c» or «p» depending on whether the measurement prior to

neoadyuvancia has been clinical or pathological (ycT, ycN, ycM or ypT, ypN, ypM), which helps us to basically decide the type of response that presented before the procedure and indirectly would help us to decide the sequence of procedures for follow-up purposes. Patients who undergo neoadjuvants do not change phase during their operation, and in such cases the initial cynic phase is the governing of the oncological performance. If a patient after procedure and independent time of pathology present recurrence of the same, the letter «r» shall be used to name the pathology, considering that the initial phase does not change with progression or recurrence (rTNM).

Once any of the elements of the pathology at the moment of beginning the categorization is unknown to us or it is not feasible to measure them in an initial way, the letter «x» is used, this only for the limits T or N; in the case of unknown M is explained as cM0, and this parameter should be used as far as possible, because it is ideal to have a correct categorization.

At the end, if the pathology is an autopsy discovery, the letter «a» prior to the properties of TNM (aTNM) shall be used to name it. All this nomenclature gives doctors in a brief way the universal information on the state of pathology.

It should be emphasized that the initial pathology phase is the most important, and once qualified does not change and this should be the one to direct the therapeutic choice to continue. Going deeper into the matter of the tumor properties mentioned in the TNM, they all change

depending on the neoplasm studied; are not the same properties of T in breast cancer to T-boundaries in renal cancer or melanoma, since all these neoplasms have modifications in survival depending on size, involvement of lymph nodes or invasion at a distance.

In what refers to the size of the lesion, the named T changes depending on the type of lesion being studied.

Logically, we can conclude that the larger the size of the tumor, the more advanced the pathology is, but this feature is not only limited to sizes, but it is also usually linked to extension in the constructions that gave them origin or the depth that invades the tissue.

In women with small breasts or men with breast cancer it is not necessary a bulging lesion to have a tumor of T4 properties and, nevertheless, the fact that the tumor invades neighboring constructions does show a fundamental prognostic translation in survival at 5 years, because it reduces from 87 to 41 per cent.

For the clinical estimation of T can be submitted to imaging studies, such as tomography, magnetic resonance imaging, ultrasound or even, in case of breast cancer, mastography. With recent cancer screening procedures, early diagnosis is more common, and we have smaller tumors to try. Because of this, the magnitudes of the injury in millimeters made the categorization into certain types

of tumours, as in breast cancer, are subdivided, and these subgroups also have prognostic significance. For example, the cT1 lesion that is defined as an injury
2 centimeters, with smaller wounds has been divided into subgroups: T1m1, which has interaction with an invasive lesion 1 mm in its largest magnitude; T1a, the one which is well over 1 mm but 5 mm; T1b, which measures 5 to 10 mm, and T1c, which could be the lesion
> 10 mm up to 20 mm.

In certain tumors, such as melanoma, the measurement of T is dependent on the depth of the lesion rather than the size of the larger shaft. In this situation, it is due to the fact that this neoplasia has fundamental affinity for lymphatic dissemination, and at greater depth, the probability of invasion and lymphatic migration increases, which represents a greater danger of scattered pathology and death.

As for the value of the N state, which explains the involvement of regional ganglia, it is a fairly fundamental element, because it represents the first degree of dissemination outside the primary tumor. In various studies carried out on different types of tumor, a deep relationship has been found between the existence of positive ganglia and the occurrence of recurrence to the pathology, the involvement of ganglia and the measurement of the lesion in general generate reduction in universal survival.

Local recurrence rate depending on tumor size, ganglion involvement and extent of surgery

	Radical mastectomy			Modified radical mastectomy		
Size of tumor in centimeters	* 2 cm	2.1-5 cm	> 5 cm	* 2 cm	2.1-5 cm	> 5 cm
Locoregional recurrence rate (%)	6.8 (3/44)	2.8 (1/36)	0 (0/4)	6.5 (4/62)	5.6 (3/54)	10.0 (1/10)
Diseased lymph nodes	0	1-3	More than 4	0	1-3	More than 4
Locoregional recurrence rate (%)	5.5 (6/109)	7.5 (5/67)	11.0 (11-57)	6.1 (11/81)	16.9 (14/83)	24.7 (18/73)

Ratio of tumor size at diagnosis and survival at 15 years according to the presence or absence of diseased lymph nodes

Size of the tumor	Average tumor size (cm)	Average tumor size (cm)	Survival after 15 years (95% CI)	Survival after 15 years (95% CI)
	Ganglion (+)	Ganglion (-)	Ganglion (+)	Ganglion (-)
0.1-1 cm	0.7	0.6	80.4 (71.2-89.6)	91.8 (88.7-94.9)
1.1-2 cm	1.7	1.6	70.1 (63.4-76.8)	89.3 (86.2-92.4)
2.1-5 cm	3.3	3.0	47.1 (40.4-53.8)	78.5 (73.4-83.6)

However, if positive lymph nodes are added, the effect is even greater. This is one of the examples of the value of grading tumors by phases. And with this justification of lower survival in patients with positive ganglia they have the possibility to suggest more energetic treatments to such patients to improve their prognosis.

As for the metastasis (M) factor, it quickly tells us about advanced pathologies, and as soon as a diagnosis of cancer is made it is necessary to make specific studies in investigation of metastatic pathology, which integrate ultrasound, tomography, MRI and even positron emission tomography.

Once we have the resources that make up the TNM categorization, the next step is to classify the tumor. Those with similar morphological properties and prognoses are grouped in teams or in so-called phases. In general, they are divided into four types of invasive pathology, which are formed by wounds ranging from better to worse prognosis and are written with roman numerals (I, II, III and IV). Phase I usually involves early wounds confined to the place of origin and show good prognosis, whereas the opposite group, phase IV, shows little response to the procedure and decreased survival. Periods II and III often describe tumors with locoregional invasion to tissues and ganglia.

The latter have the possibility to subdivide into sub-groups depending on forecast components. Separate mention has phase 0, which is assigned to wounds limited to wounds in situ and are considered non-invasive. Based on these results, it can be seen why certain teams of patients with a suitable prognosis limit the procedure to local control, such as surgical performance only, and to patients with limited survival, the treatments may be more aggressive in order to minimize the risk of relapse or death from cancer.

Non-anatomical prognostic factors

As explained above, in the TNM only anatomical expansion limits are taken to classify a neoplasia; However, there are other properties of the tumor that influence the prognosis and outcome of treatments, including the level of cell differentiation and the biological profile of the tumor.

The level of cell differentiation is a scoring scale that suggests at what level the appearance of cancer cells differs from typical cells.

Mainly split in degrees (usually three): neoplastic cells with more like a usual cell will be called either differentiated or level I; Level II cells are moderately differentiated in relation to the cell that gave them origin, whereas poorly differentiated or Level III cells are lesions with little resemblance to the cells of the tissue that gave them origin. The element of low differentiation is poor prognosis, so even though it is not included in the TNM, it is necessary to express it to explain a neoplasia.

These other properties argue that neoplasms having the same phase show different treatment results. The mixture of overexpression of some or all of these receptors can influence boundaries such as relapse of pathology or universal survival, so that the reasoning of such limits is currently leading apart from etapification to normalize the patient's procedure.

Other markers of cell proliferation, as part of the S stage, mitotic index, Ki-67, mutation study of genes such as EGFR, Kras and overexpression of the ALK gene, are also biological properties that have demonstrated effect on the prognosis of pathology. Today, all these biological markers are essential for making therapeutic choices.

PRINCIPLES OF CANCER SURGERY

Today, surgery continues to be the most effective therapeutic for cancer, with the highest cure rate despite significant advances in the field of radiation therapy, chemotherapy, Therefore, surgery is an important part of the multidisciplinary functioning of cancer, because it participates in prevention, diagnosis, staging, healing procedure, palliation, complications and consequences.

The oncologist surgeon not only has the technical ability to make the oncological surgical method, but also knows the biology of the tumor, the head of dissemination and should coordinate the multidisciplinary set to be able to make the greatest triumph in the procedure. In the end, it has been shown that the greater the number of cases treated by a surgeon, the greater the experience, the better the immediate results (lower morbidity and mortality) and increases universal survival, which is a necessary objective for the oncological outcome. Therefore, surgical accessories for cancer will have to have experience in the tumor

to try, to increase the success in the procedure, and if this is not feasible, it is preferable to refer the patient with the appropriate equipment so as not to deteriorate the probability of healing and quality of life.

CANCER PREVENTION SURGERY

In addition, so-called danger reducing or prophylactic surgery, it is done on premalignant wounds or hereditary syndromes that predispose to cancer and its objective is to anticipate the onset of the pathology, emphasizing the actual benefit and potential danger of the method in a healthy patient but which may have long-term consequences for the surgical method.

In breast, the premalignant lesion is ductal carcinoma in situ, and total mastectomy with instant recomposition prevents progression to an invasive tumor with a convenient aesthetic outcome. In the identification of BRCA1 and BRCA2 mutations, which predispose to hereditary breast cancer by 56-84% and which are early, bilateral and aggressive tumors, danger-reducing bilateral mastectomy is indicated, which reduces the risk of breast cancer by up to 90% and does not require axillary dissection.

SURGERY IN CANCER DIAGNOSIS AND STAGING

To confirm the diagnosis of malignancy it is very important to have a histopathological study, and for that you need a biopsy or sample of suspicious tissue, which will be sufficient, without contaminating tissues

adjacent, uncomplicated and with an optimal incision for planning the final procedure, so it will have to be developed by an oncologist surgeon.

The stadification or expansion of pathology is important in determining the procedure and prognosis; Depending on the type of tumor and clinical stage, the primary tumor may be resected at first and then offered a complementary procedure. On other occasions, once the tumor is not resectable, surgery will only confirm the diagnosis and then start the procedure with chemotherapy and/or radiation therapy.

SURGERY IN CANCER TREATMENT

Surgery is the mainstay of the oncological procedure and has the highest cure rates for firm tumors, even though in past decades it was considered mutilating.

Less extensive but accurate resections are currently performed to achieve the primary purpose, which is locoregional tumor control with the greatest organ preservation and functionality for the patient. An excellent example is breast conserving surgery in well-selected patients, which is conducted to tumor excision with negative margins and later complementary radiotherapy is added. With this approach, the breast is aesthetically acceptable, there is a low risk of recurrence, and survival is similar to vision with extreme mastectomy.

The term surgery with curative intent aims to completely erase the primary tumor and regional ganglia with negative margins without evidence of metastatic pathology, so a deep understanding of tumor biology is necessary to plan the best surgery, because the first surgical procedure has the greatest chance of success, and ill-indicated surgery limits ways for local control, restricts organ preservation and reduces the likelihood of healing, the basis on which surgical principles in oncological surgery have been postulated.

Surgical principles in oncological surgery
Any resection of the primary tumor should have a free three-dimensional margin and regional ganglia should be added
The ganglion dissection should be in a centripetal direction with respect to the primary tumor
Early vascular control should be carried out during the surgical examination, the edges of the abdominal wall should be protected and manipulation or rupture of the tumor should be avoided to decrease implantation of tumour cells
During the surgical evaluation it should be determined if the tumor is resectable, since a surgery with macroscopic residual tumor plus secondary morbidity does not benefit the patient
After tumor resection the surgical field should be washed to lyse residual tumor cells

In curative surgery, the definition of complete resection is referred to as «R0», which means complete tumor removal with negative or free margins in histopathological report, a resection «R1» assumes that there are positive margins under the microscope despite having no visible tumor throughout the resection and a «R2» resection assumes that there is residual visible (macroscopic) tumor at the site of the resection.

Another criterion in oncological surgery is that of unresectable tumor, which is used once, by location, size

or expansion is impossible to achieve complete resection and margins are involved. In the end, the inoperable concept is used once the patient's physical condition or comorbidities do not allow surgery despite having a resectable tumor.

Examples of irresectability and inoperability

Irresectability	Inoperability
Gastric tumor spreading and envelops the vessels of the celiac trunk or with the presence of carcinomatosis and malignant ascites	Liver cancer with poor functional reserve secondary to cirrhosis
Ganglion conglomerates fixed to cervical vertebrae or surrounding carotid vessels	Extensive kidney cancer in single kidney, no chance for kidney transplant
Retroperitoneal sarcoma fixed to the spine or with extensive vascular infiltration	Lung cancer or mesothelioma
Lung cancer with invasion of mediastinal vessels, trachea and malignant pleural effusion	Spinal metastasis with paraplegia by medullary compression and other sites of metastatic disease
Tumor in head and neck that invades brain, base of skull or both orbits	Patient with considerable morbidity as a antecedent of acute myocardial infarction and poor functional status

At present, significant advances have been made in minimally invasive surgery for cancer that have demonstrated the same oncological outcome (radicity, margins and prognosis) when compared to open surgery, which is the standard, but with the benefit of less surgical bleeding, less pain, shorter hospital stay and immediate postoperative recovery.

SURGERY IN COMPLICATIONS AND CONSEQUENCES OF CANCER

Every cancer patient is in danger of exposing complications throughout the course of the pathology, whether following the healing procedure or as part of an advanced stage. Gastrointestinal or gynecological tumors have the possibility of intestinal obstruction, perforation, bleeding, anastomosis dehiscence, among others, so the surgeon will have to be prepared to approach such patients and not forget that they have the possibility of having past treatments with radiation therapy, chemotherapy and/ or surgery, which makes it difficult to try these complications. Chemotherapy in gastrointestinal lymphomas has danger of creating perforations, radiotherapy for tumors of the cervix or rectum creates proctitis, which increases the danger of necrosis or perforation, and eventually osteoradionecrosis in head and neck will require debridement and early recomposition.

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CHAPTER: 3

MORBI-MORTALITY: BREAST CANCER.

INTRODUCTION

Breast cancer has now become not only a medical and public health problem for all nations around the world, but it has an economic, political and social impact on each of these entities. In addition, their understanding for convenient detection and correct referencing is not unique to the oncological specialty; on the other hand, it should include all members of the health system, including doctors and paramedics, in order to combat this pathology more efficiently and effectively, and achieve the desired goals of disease control more quickly and thus improve the prognosis of patients with this public health problem.

Epidemiology

Worldwide, breast cancer is a public health problem. It is the primary cause of cancer diagnosis in the lady and the first cause of death for this pathology. They are diagnosed annually
1.6 million women, reporting well over 500,000 deaths. It represents about 25% of the total cancers diagnosed in the lady.

There is a wide variety in the incidence rate depending on the territory of the whole world in which it is located. The highest incidence is shown in North America and Western Europe, with incidences of well over 80/100,000 inhabitants, being the USA. and Australia the nations of greatest incidence; On the European continent, the main territories are in the Western bloc, with France and Denmark. In the U.S. 240,000 patients are diagnosed annually, with well over 40,000 deaths, corresponding to 14% of the lady's total cancers. In Latin America an intermediate incidence is reported, with 28/100,000 inhabitants, which is very similar to the one reported in our region.

HAZARD FACTORS

It is accepted that breast cancer has a genetic origin which, in mixture with other various components such as female gender, age, previous relatives, environmental, lifestyle, exposure to both endogenous and exogenous female reproductive hormones, benign pathology of the breast, reproductive history, obesity and other changing, produces the appearance of pathology. It is estimated that about 50% of women

who develop breast cancer do not have any identifiable element of danger beyond the age and gender of women, these two components of danger being the most prominent. This pathology is 100 times more common in women than men and increases substantially with age: from less than 10 cases/100,000 females per year between 20 and 30 years of age, to well over 300 cases/100,000 females per year greater than 60 years.

SCREENING AND APPROPRIATE DETECTION

The fundamental objective of screening this pathology is adequate detection to minimize mortality, which develops from the examination for the detection of danger components and clinical analysis, We then support ourselves with mastography and other aids for diagnosis, such as ultrasound and magnetic resonance imaging, in cases that require complementation for the characterization of wounds or to believe in malignancy. The studies most commonly used to screen pathology are described below:

- Mastography: it is the exclusive analysis that has decreased mortality up to 30% in the population in which the screening was carried out, allowing an early diagnosis and a procedure. Two projections are made: cephalocaudal and half-lateral oblique. The indication is in women asymptomatic from 40 years old, in ladies who show dense breasts, palpable injury, previous to breast cancer, secretion by the nipple, changes in the dermis or nipple, breast cancer cree, family history of cancer starting at 30 years or 10 years

history of the cancer family member's age.

- Breast ultrasound: not an effective screening instrument; However, it is used in women under 35 years with breast pathology, dense breast, characterization of visible lesion in mastography, breast implants, infectious processes and guide to make methods (biopsy, drainage of abscesses and aspiration of cysts).
- Resonance magnetic:
  Complementary procedure to mastography and ultrasound. It is mainly used in the assessment of disease expansion, as well as in the postoperative to assess margins, local recurrence and response to procedure, although it is expensive for routine use for these purposes; in primary occlusion investigation with axillary metastases, pregnancy, dense breasts, guided biopsies of non-ultrasound visible wounds, on breast implants and some special occasions for convenient detection.

There are other tools for the proper detection of this pathology, such as tomosynthesis, elastography and positron emission mastography, which are complementary studies to those already mentioned.

The analysis categorized as 0 is inconclusive and needs further projections or studies; Category 1 and 2 need to be monitored annually; 3 needs six-monthly follow-up; 4 and 5 need biopsy, and at the end category 6 corresponds to a breast cancer already confirmed by biopsy.

CLINICAL STUDY

The widespread use of studies such as ultrasound or mastography has increased the detection of malignant wounds prior to causing any symptoms. Even in this way, certain cancers are not detected by means of these, and then a careful physical investigation and a descriptive clinical interrogation is elementary. Breast self-examination is based on the palpation of both mammary glands by our patient and is offered to be performed throughout the shower on days 7 and 10 after menstruation. This procedure has a sensitivity of 26-41% identifying wounds 0.5-1 centimeters in diameter in up to 65% of the women who use it. Physical testing by medical or nursing personnel trained in the subject begins at age 25 on an annual basis and has a sensitivity of 40-69% and specificity of 88-99%. Begin by examining the patient in a sitting position, detecting changes in the nipple, asymmetries and masses, subtle changes in the dermis, dimples or orange skin, as well as erythema or fine appearance, which remain associated with locally advanced pathology or inflammatory cancer. In breast palpation the patient places both arms behind the head.

It can be done in a circular fashion or by following the clock. In giant or ptosis breasts, the breast could be raised making it easier to inspect the lower amount of the same, reporting the appearance of the lesion found, its size, shape, location, consistency and mobility. At the end, the axillary, cervical and clavicular lymphatic chains are evaluated for pathology, and the number, size and mobility are characterized

of damaged ganglia, because 55-85% of cases show palpable metastases to axillary or supraclavicular nodules at the time of diagnosis.

The most common signs that are shown in the anamnesis and physical investigation of a patient with this pathology is the detection of mammary nodules, secretion by the nipple, cutaneous alterations such as retraction of the dermis of the breast and more rarely detection of axillary or supraclavicular ganglia, as well as weight loss.

DIAGNÓSTICO

The diagnosis of breast cancer is based on the evaluation of clinical and radiological data, and histological confirmation of the lesion, which could be palpable or detected by imaging. Percutaneous biopsies are preferred to incisional or surgical, because they have better aesthetic results, lower prices, are less morbid and allow, in the case of cancer, the idealization of the procedure, Considering that in the face of malignancy, the biopsy should be carried out at the center where the patient will receive the definitive procedure in order to have a better organization of it. Palpable wounds have the possibility of developing without imaging, and once we talk about non-palpable wounds, they have the possibility of being guided by ultrasound, in case of cysts or nodules, and in case of microcalcifications the best procedure is guided by sterotaxy with mastography.

The wounds have the possibility of being biopsied by fine needle aspiration, whose largest implementation

is in the analysis of suspect axillary ganglia, because tissue collection may not be sufficient in breast wounds, as well as the inability to distinguish between in situ and invasive wounds, in addition to the high rate of non-diagnostic or erroneous positive samples. Biopsy with a cutting needle makes it possible to obtain material suitable for the diagnosis of breast wounds and can be carried out with vacuum aid, which enables the extraction of a larger proportion of tissue; However, special sets are required for this procedure and are preferred in the case of microcalcifications.

Once the complete subtraction of the lesion is made, a clip must be placed throughout the biopsy to mark the site and take it for future complementary treatments. Incisional biopsy will be indicated once the above instruments are not available or once the clinical thinking is high for malignancy and we have negative results from other procedures.

All patients need a chest teleradiogram and, in addition to the above, patients who are thought to be locally advanced will require expansion studies to assess the likelihood of metastatic pathology, Bone imaging and hepatic ultrasound are the most used, although in some cases it is necessary to implement a positron emission tomography to evaluate this expansion more efficiently.

Stadification

The staging of breast cancer is done through TNM categorization, an initiative by the American Joint Committee on Cancer. It is effective in making the patient analysis protocol, provides information regarding prognosis and serves to guide the procedure. Patients with EC I and II or centimeter tumors have a low probability of undergoing metastatic pathology, so it is not recommended to conduct expansion studies routinely. There is a clinical and a pathological categorization, and the latter is used after having sent the surgical biopsy to histopathological analysis.

HISTOPATHOLOGY AND MOLECULAR CATEGORIZATION

Histopathology

The WHO histological categorization (WHO) is the most widely used for invasive breast cancers.

Invasive ductal carcinomas represent the most recurrent set of invasive breast cancers, with 70-80%, and have several synonyms for their identification, including easy and spheroidal cell carcinoma.

Invasive lobular carcinomas are the second most recurrent type of invasive breast cancer, with 5-10%. The increase in the frequency of its presentation has been related to the use of hormone replacement therapy in postmenopause. Lobular carcinoma in situ coexists with invasive lobular carcinoma in 70-80% of cases. World Health Organization

proposed to classify metaplastic carcinomas as pure epithelial or mixed epithelial and mesenchymal.

Molecular classification

Alterations of genes associated with breast cancer were performed using bioinformatics, molecular biology and genomic techniques, which allowed to find different oncogenes and tumor suppressor genes associated with this neoplasm, one of the main being HER2/neu. The expression of estrogen and progesterone receptors generally have a better prognosis than negative ones

SURGICAL TREATMENT

The surgical operation in these phases can be divided into:

- Conservative procedure: has interaction with a three-dimensional resection of the primary tumor and surrounding healthy tissue, with free margins of tumor. It can be considered in patients who do not have multicentricity data, who have an ideal breast-tumor relationship and who agree to receive radiotherapy to the breast after surgery.
- Extreme procedure: basically refers to doing a mastectomy in its different possibilities.
- Conservative surgery with extreme dissection of the armpit: this is related to a three-dimensional resection of the primary tumor and surrounding healthy tissue.
- Modified extreme mastectomy: which is supported

in the removal of all breast tissue, as well as axillary ganglion dissection. In the end, the procedure for metastatic breast cancer is merely palliative; However, the surgical procedure can be evaluated in 3 scenarios:

- Resection of metastatic pathology, mainly pulmonary and/or hepatic.
- Resection of the primary breast tumor in the presence of bone oligometastasis.
- Palliative resection of the breast tumor in the presence of ulceration or bleeding.

Treatment

In recent years, enormous progress has been made in the diagnosis and treatment of breast cancer, and cytotoxic therapy and radiotherapy have succeeded in improving the independent time of progression and universal survival as in no other neoplasia worldwide, composed of adjuvant, neoadjuvant and palliative treatments as well as the management of hormone therapy in hormone-sensitive tumors and white therapy in HER2/neu overexpressed tumors.

- Cytotoxic procedure: currently, the standard schemes of choice, whether adjuvant or neoadjuvant, are based on anthracyclines. The most used schemes are based on adriamycin + cyclophosphamide for 4 continuous cycles of a taxane (paclitaxel/docetaxel) for 4 cycles or management of 5-fluorouracil + adriamycin or epirubicin + cyclophosphamide for 3 or 4 cycles.
- Hormone therapy: the standard procedure in

premenopausal patients is tamoxifen 20 milligrams orally daily over 5 years; and in postmenopausal women, based on aromatase inhibitors for 5 years. There are currently studies supporting the work of tamoxifen with or without anastrozole for up to 10 years in specific cases.

- Anti-HER2/neu therapy: should be part of the adjuvant procedure for patients with tumors that overexpress the HER2/neu protein, because it reduces annual relapse by up to 50%. The most common procedure is trastuzumab for one year. It does not have to be ruled together with anthracyclines for the cardiotoxicity of both and can be used together with hormone therapy and radiotherapy.
- Radiotherapy: its work reduces the possibility of local recurrence of the tumor, irradiating the chest wall, mastectomy mark and drainage holes, typically receiving a dose of 45-50.4 Gy in 25-28 fractions.

METASTATIC STAGE

Of all breast cancer cases, a third will occasionally have metastatic pathology. Fortunately, only 5% worldwide and 9.6% in our region are initially diagnosed in this period, of which 75% will die at 5 years.

The associated components for the development of this phase is the ganglion state, because of the patients who initially had localized pathology to the breast, the number of ganglia is the predictor of recurrence

locoregional and distance more relevant and survival, being 83% at 5 years in the case of axillary ganglia negative and 28% in those with well over 13 positive ganglions.

Tumors with positive hormone receptors usually expose to bone or locoregional spread, with better prognosis, while patients with triple negative tumors or with overexpression of HER2/neu have higher rates of visceral and cerebral metastases, respectively, with the lowest 5-year survival. The most common sites of distant metastasis are lung (71%), liver (71%) and bone (62%).

Performance will depend on the age and serviceability of the patient, as well as the molecular subtype. Performance has no curative goals, but palliative ones, and the goal is to improve the quality of life.

Chemotherapy is going to be used in tumors with negative receptors; patients with positive hormone receptors will be treated with hormonal therapy based regimens, and in the situation of overexpression of HER2/neu, depending on the previous procedure, there is even double anti-HER2/ neu block. Especially for bone metastases, patients are preferably treated with bisphosphonates to prevent pathological fractures, although in case of pain or believe of medulla radiation therapy is the valid alternative. For visceral metastases, performance is specific to the molecular and palliative subtype, with methods such as thoracentesis, paracentesis and bile duct derivations.

In the situation of metastasis to the central nervous system, several are candidates for radiosurgery or holocranial radiation therapy, with an average survival of 4-6 months and relevant consequences. Primary tumor surgery is a controversial issue that does not yet show improved survival; However, it is indicated in cases of ulceration or bleeding.

Follow up

Upon completion of the primary breast cancer procedure, the monitoring and control phase called follow-up begins. The internationally accepted suggestions for follow-up of these patients are then described. It is essential to point out that trying to anticipate the diagnosis of metastatic activity does not increase survival or quality of life, so it is not indicated to do routine tests.

RISK REDUCTION THERAPIES

The hazard components for the development of breast cancer are already well known, and therefore effective breast cancer risk reduction tactics such as the use of hazard-reducing agents and hazard-reducing surgery have been recognized, in patients with known genetic mutations. Surgical hazard reduction tactics have the potential to have psychosocial and/or physical sequelae for the lady, and the hazard reducing agents used in non-surgical hazard reduction remain associated with certain adverse effects.

- Lifestyle modifications: diet, exercise, body weight control and decreased alcohol consumption have not been shown to have scientific evidence that guarantees a decrease in breast cancer.

Risk reduction surgery:

-- Bilateral total mastectomy: the risk for breast cancer in BRCA1 or BRCA2 mutation carriers has been estimated at 56-84%.

- Hazard reducing agents: tamoxifen, raloxifene, anastrozole and exemestane only for females over 35 years of age; the usefulness of these agents in women under 35 years old is unknown.

GENETICS AND BREAST CANCER

The family history of breast cancer is considered a danger component for the development of this pathology; However, only 5-10% of the population diagnosed with this pathology has a true genetic element.

The previous breast cancer in the mother or a sister is increased the risk of breast cancer by 1.5-3 times above general population and it is estimated an element of danger with heterogeneous repercussions, because it will be modified by situations such as the precise interaction of the injured family member, the number of patients with breast cancer in a family and the age at the time of diagnosis of the damage.

There are certain conditions that can lead us to think we are dealing with a case of hereditary breast cancer:

- At least 2 first-level relatives with breast cancer, one of them diagnosed before age 50.
- 3 or more first- or second-level relatives with breast cancer, at any age.
- Prior to breast or ovarian cancer among first and second level relatives.
- First-level family member with bilateral breast cancer.
- Breast cancer in men.
- 2 or more first- or second-level relatives with ovarian cancer.

There are different genes involved in the pathogenesis of hereditary breast cancer, among which the most relevant are BRCA1 and BRCA2, consecutive by PTEN, TP53 and ATM, and that cause different syndromes of the genes, as explained below:

- BRCA1 and BRCA2: mutations in these genes are inherited autosomally dominant and found on the 17q21 and 13q chromosomes, respectively.
- PTEN: Cowden pathology caused by the PTEN mutation is inherited in an autosomal dominant manner and is characterized by various wounds, such as hamartomas of the digestive tract, trichilemomas, papillomatosis of lips and oral mucosa, thyroid cancer, uterine fibroids, and cysts

and ovarian cancers.

- TP53: p53 is a tumor suppressor gene located on chromosome 17p13. This mutation is implicated in Li-Fraumeni syndrome, which poses a high risk of exposing breast cancer, osteosarcoma, soft tissue sarcoma, brain tumors, leukemia and adrenocortical carcinomas.

It is estimated that 1% of breast cancer cases remain involved with this mutation, and it is the most frequently associated cancer, with a breast cancer risk of 56% for 45 years old and greater than 90% for 60 years old.

- ATM: ataxia-telangiectasia is a genetic disorder characterized by oculocutaneous telangiectasias, cerebellar ataxia, immunodeficiencies and predisposition to lymphoma and leukemia.
- There are genes of lower penetrance that are also involved in hereditary breast cancer, although to a lesser extent, such as CHEK2, CDH1, PALB2, BRIP1 and RAD51D, among others.

CHAPTER: 4

MORBI-MORTALITY
UPPER: LUNG CANCER.

Epidemiology

Lung cancer (PC), a rare disease in the early 20th century, is now one of the most common worldwide, with almost 2,000,000 cases diagnosed during the 2010s. The incidence of PC is dependent on changes such as age, gender, ethnicity, socio-economic status and geographical location. Mortality is alarming, with 1.6 million fatal cases recorded in this stage of time on the planet, which means that one in five deaths from cancer is due to this entity. Mortality rates across the globe are uneven, with a downward trend in developed territories such as Canada, the US, England and Australia, a marked trend since the 1970s. This is also true for certain developing territories.

However, incidence and mortality rates are still rising in other developing territories in Africa, Asia and South America where the beginning of smoking was subjectively late.

Etiology

Smoking as a major hazard component for lung cancer.

In more than 80% of cases in men and 50% of cases in women, tobacco is the cause of CP4 development. This grouping was established in 1964 by the Emerge General's Report, with a desirable effect on public health.

It is believed that 1.3 billion individuals around the world smoke. This addiction has a downward behavior in developed territories; However, it has been preserved or even increased in developing territories.

Well over 8,000 compounds in tobacco and the smoke it creates have been characterized, of which 70 are classified as carcinogens by the International Agency for Research on Cancer. The most relevant are polycyclic aromatic hydrocarbons, aromatic amines, volatile nitrosamines, aldehydes and volatile hydrocarbons, metals (nickel, arsenic and chromium), the radioelement 210Po and other organic resources. The key piece in tobacco carcinogenesis is formed DNA adducts.

These are usually terminated by DNA base repair enzyme systems. However, if these are inefficient or exceeded, DNA adducts cause miscoding, with mutation of tumor suppressor genes such as TP53, RASSF1A and FHIT. In this process they also have the possibility of intervening certain epigenetics that favor malignant transformation. Other lung cancer hazard components other than smoking: biomass exposure, air pollution and radon exposure.

There are other hazard components that need to be kept in mind in non-smoking patients with PC. The concentration of these pollutants in the environment, including ozone, nitrogen dioxide, sulphur dioxide and particulate matter (PM) («particulate matter»), is dependent on vehicle fleet, plant emissions and the direction of air currents.

These contaminants were associated with increased risk of various types of cancer. Globally, it is estimated that 19 per cent of each cancer is attributable to the environment, resulting in about 1.3 million deaths annually.

Another hazard associated with PC is exposure to radon, an inert gas produced from uranium decay and a major environmental cause of PC. Radon is present in soil, stones and groundwater and can be collected at home. The decay products of radon, polonium 218 and polonium 214, are capable of producing particles α, some

high-energy, high-mass particles consisting of 2 protons and 2 neutrons causing mutations in DNA bases and breaks in the chromosomal chain linked to their carcinogenic potential

Regarding the components of the CP genes, the EAGLE analysis highlights that the relative risk of CP associated with a positive family history, adjusted for age, sex, residence, education and smoking, was 1.57 (95% CI: 1.25-1.98). In non-smokers with PC, a susceptibility locus has been suggested. The sites located as possible are chromosomes 6q, 5p15. (TERT), 13q31. (GPC5), 15q25 and 6p215.

Clinical picture of lung cancer

The most common signs of PC are generalized exhaustion, fatigue, weight loss, coughing, hemoptotic expectoration and dyspnea, all of which are associated with a local increase in neoplasm. Other patients will have indications regarding the sites of metastatic pathology, such as bone pain, headache or preeminent vena cava syndrome, among others. Eventually, some patients may develop paraneoplastic syndromes. Up to 10% of patients are likely to be asymptomatic.

Diagnosis and staging of lung cancer

PC represents a diagnostic challenge that usually begins with a lung lump or nodule on a chest plate. The subsequent analysis indicated is a chest CT scan, which makes it possible to assess the local

pathology and viable mediastinal involvement. Then the histological diagnosis is necessary. For this the location of the tumour is decisive. In the peripheral wound situation, ultrasound-guided biopsy or tru-cut tomography is preferred.

Bronchoscopy is preferred for central wounds. The stapification of mediastinum is important. The gold standard is mediastinoscopy; However, positron emission computed tomography (PET-CT) can also be used. If CT and PET are negative, mediastinoscopy may be omitted; However, any abnormal image result should be confirmed by disease. Even if mediastinoscopy is not done, the mediastinum ganglia have to be evaluated throughout the surgical method. In patients with low risk of mediastinal pathology with N1 ganglia (iliary and peribronchial ipsilateral) endobronchial ultrasound can be used. CT or MRI of the skull remain recommended in patients with positive ganglia or signs of central nervous system.

TREATMENT OF LOCALIZED AND LOCALLY ADVANCED PHASES

Treatment of lung cancer in clinical stages I and II

About 30% of the patients with PC are in these phases, whose initial procedure is based on surgery with curative intent; lobectomy was chosen, which showed lower rates of local recurrence and higher survival.

In addition, it should integrate lymph node dissection that integrates bronchial, hilar and mediastinal ganglia according to location and laterality. However, despite the surgical procedure a significant number of patients will have recurrence and occasionally die from the pathology, so an adjuvant plan with chemotherapy is born as a maneuver to increase survival.

For PC artificial intelligence periods post-surgery chemotherapy showed no benefit and was associated with worse survival, and for IB periods adjuvant chemotherapy (QA) only showed benefit in the subgroup of patients with 4 cm tumors. The current recommendation is to perform QA with platinum-based regimens (better results with vinorelbine-cisplatin) in patients with fully resected clinical stages II and IIIA.

Etapa III

The irresectable phase III procedure is based on definitive concomitant chemoradiation therapy (QTRT), in which radiation therapy gives local control, and chemotherapy (platinum-based scheme), functioning of micrometastatic pathology and also serves as a radiosensitizer.

The absolute benefit of concomitant QTRT in universal survival (OS) is 4.5% at 5 years and 6.1% in locoregional progression at 5 years. In order to increase the systemic control of the pathology, induction or consolidation chemotherapy was proposed in partnership with QTRT, obtaining negative results in survival and increasing toxicity.

The resectable pathology refers, generally, to phase IIIA not large, whose procedure is controversial but directed to local control (surgery and/or radiotherapy) and then systemic functioning with chemotherapy. The probable combinations include surgery followed by QA with or without radiation therapy, neoadjuvant chemotherapy followed by surgery and QTRT. However, until then it was not demonstrated superiority of one local plan over the other in SG. In case of N2 discovery following surgery, QA followed by adjuvant radiation therapy is offered.

Procedure for metastatic lung cancer

One of the most dynamic topics on the CP agenda is clearly the advanced pathology procedure. In the last 2 decades we have observed the transition from non-personalized treatments of type cytotoxic chemotherapy to targeted therapies sites of cellular signaling pathways, i.e., white (TB) therapies, and then return to non-personalized treatments that activate T cells so that they have an impact on neoplastic cells, in other words, immunotherapy (IT).

IT not only differs in the mechanisms of action, but also in the profile of adverse attitudes that need special monitoring and understanding by staff working with cancer patients. This section is a brief historical review in the therapeutic of metastatic CP.

Role of chemotherapy in the metastatic lung cancer procedure

The purpose of the procedure in patients with advanced PC is to improve quality of life and prolong survival. Studies with 2 chemotherapy drugs, which in the CP continuously integrate a platinum, have response rates of pathology ranging from 17 to 32%.

Adverse changes are diverse among the different chemotherapy regimens available, so it is proposed to adjust to the patient's preferences, age and comorbidities.

White therapy in the advanced lung cancer procedure

The development of TB has as conjecture that CP is a heterogeneous pathology, subcategorized by driver mutations that predict TB response. The most relevant mutations for their frequency and the availability of drugs against them are EGFR and ALK.

For patients with adenocarcinoma of the lung with ALK mutation, present in 2-7%, crizotinib, alectinib and ceritinib have shown superior oncologic outcomes over common chemotherapy and conform in advanced lung cancer immunotherapy

The immune system (IS) plays a key role in cancer control. The probable scenarios of the tumor-immune system relationship are suppression, balance, flight and avoidance to immune devastation. Tumor cells manifest different mechanisms that prevent autoimmunity in classical cells and are thought to be evasion mechanisms.

CHAPTER: 5

MORBI-MORTALITY
UPPER: COLORECTAL CANCER.

Colon and rectal cancer ranks third in the world, with about 1.2 million new cases, behind lung and breast cancer. Every year, colon and rectal cancer is responsible for a little over 600,000 deaths on the planet.

Etiology

Epidemiological studies suggest that colorectal cancer is due, in particular, to dietary components. It has been pointed out that fat is involved in the promotion of carcinogenesis, and type and quality are important. The population that consumes large portions of fat has greater secretion of bile salts and higher incidence of colorectal cancer. Other components such as high alcohol consumption, smoking and obesity also increase the risk of

colorectal cancer. In contrast, other components such as the exuberant intake of fiber, calcium, vitamins C and E, selenium and nonsteroidal anti-inflammatory drugs decrease the danger.

Due to its clinical, epidemiological and genetic properties, the following types of colorectal cancer are distinguished: sporadic (70-80% of cancers of the colon and rectum), familial, hereditary and referent with inflammatory pathologies, such as chronic nonspecific ulcerative colitis (CUCI) and Crohn's disease.

Hereditary cancer is subdivided into 2 monumental syndromes:

- The one associated with polyposis (such as familial adenomatous polyposis and hamartomatous polyposis syndromes, such as Cowden syndrome and its versions -Bannayan-Riley-Rubalcaba syndrome, juvenile polyposis syndrome and Peutz-Jeghers syndrome).
- He who lacks those polyps. The latter syndrome without polyposis is transmitted in an autosomal dominant way and explains 2-10% of colorectal neoplasms. There is an exception between the syndromes of Lynch I (isolated colorectal cancer) and Lynch II (colorectal cancer linked with cancer of stomach, small intestine, endometrium, ovary, urothelium, liver and bile ducts).

About 5% of the population under 50 have adenomatous polyps in the colon or rectum, and after 70 years these frequencies increase to 30%. Succession has been notified

or progression from adenoma to carcinoma. Other carcinogenicity routes are now known, such as de novo and flat or inverted polyp. The resection of polyps has been shown to reduce the chance of developing colorectal cancer. The magnitude of the polyp and the existence of chromosomal abnormalities influence its malignancy capacity. A huge set of genes is involved in carcinogenesis and refers to an imbalance between suppressor and oncogenic genes.

PREVENTION

The primary primary prevention measure could be achieved by modifying dietary components, with low intake of fats and high intake of fruit and vegetable fibers, in addition to routine physical exercise. Secondary prevention is aimed at patients with pre-malignant wounds to minimize the danger of their conversion to malignancy.

Medical performance with supplements with calcium and vitamin D, or anti-inflammatory drugs such as aspirin or is directed have shown reduced hazard in patients with adenoma, or surgical procedure such as polypectomy, total colectomy or proctocolectomy in subjects with familial adenomatous polyposis and total colectomy in carriers of mutations in the hereditary colorectal cancer syndrome without polyposis.

PATHOLOGICAL ANATOMY

95% of malignant neoplasms are adenocarcinomas. Other unusual neoplasms are the

neuroendocrine tumor, sarcomas, lymphomas and gastrointestinal stroma tumor. 2-thirds of cases occur in the left colon and a third in the right. About 20% develop in the rectum, although in recent years there has been an increase in the number of cases located in the rectum, reaching up to 50%.

CLINICAL PICTURE

Although the large intestine is a single composition, the signs and prognosis are different depending on the location of the cancer. Malicious tumors of the right colon grow locally to huge magnitudes without causing intestinal obstruction, as a result there are liquid feces and enormous distensibility of this segment of the colon. Signs are vague abdominal pain, fatigue and weight loss, and several months later the mass and clinical data of anemic syndrome will be palpated.

Tumors of the left colon are frequently shown with symptoms of partial or complete intestinal obstruction, such as deep colic pain, decreased stool caliber and hematochecia. If located in the rectum, constipation and bleeding will be the most important signs, being even accessible to the digital study. So, the age of evolution from when signs begin to diagnosis is less in tumors of the left side.

Metastases to regional ganglia remain present in 40-70% of cases at the time of resection, and venous invasion passes in up to 60% of cases. Often, metastases are affecting the liver

(40-60%), peritoneal cavity (30-40%) and lung (30%), consecutive of the adrenal glands, ovaries and bones.

Cancers of the rectum spread through the inferior vena cava (as opposed to the venous drainage of the colon, which is located in the portal vein); Because of this, rectal cancer metastasizes to the lungs.

DIAGNÓSTICO

In addition to the complete history, diagnostic maneuvers include rectal touch, which is effective for tumors located in the distal third of the rectum. Physical research will reveal the properties of the tumor, its interaction with the pelvis and neighboring organs, as well as the likelihood of documenting tumour activity at the bottom of the Douglas sac. Colonoscopy is the diagnostic test of choice. With it they have the possibility of visualizing completely the colon and rectum, and makes it possible to take biopsies of the tumor and identify synchronic tumors.

As expansion studies are recommended a chest X-ray, computed tomography of the belly and pelvis (including thorax in cases of rectal cancer), magnetic resonance imaging of the liver in case of doubt of liver lesions and, recently, the use of positron-emission computed tomography in selected cases. We must decide the levels of the tumor marker carcinoembryonic antigen (CEA) in blood and other blood studies, such as blood biometrics and complete blood chemistry.

ETAPIFICACIÓN

After the histological diagnosis is made, it is essential in most patients to establish the expansion of pathology (also known as cancer stages). The stage is directly correlated with the level of development of pathology and prognosis.

MOLECULAR BIOMARKERS

Several molecular alterations were identified in patients with colorectal cancer, being the primary mutations in the oncogenes KRAS, NRAS, BRAF, PI3KCA and MET and microsatellite instability (MSI), HER2/neu, thymidilate synthetase, MET and DPD, among others.

These biomarkers have been recognized and examined in patients with metastatic colorectal cancer. Those with practical utility are, so far, the non-mutation of KRAS and NRAS (predictor of response to anti-receptor therapy of the epidermal augmentation component [EGFR], present in 50% of patients) and the decision of the MSI (predictor of response to immunotherapy), this in tumoral tissue (preferably in the primary tumor). The mutation in BRAF represents the worst component of poor prognosis, since, despite a systemic procedure, its average survival is less than 12 months. The biomarkers that we must decide before deciding the systemic oncological procedure in metastatic colorectal cancer are KRAS and NRAS.

Treatment

Surgery

The oncological procedure is multidisciplinary, but surgical mediation has several purposes:

- Diagnosis: once you can not have a sample of the tumor in the colon or is insufficient, biopsy should be taken by puncture or open.
- Therapeutic: once the primary tumor is dry (consensus intestinal resection to the site of the colon where the tumor is located).
- Prognosis: if a complete resection is achieved, the prognosis is better.
- Prophylaxis: in cases of presence of premalignant wounds, such as hairy adenomas or adenomatous polyps, among others, a prophylactic intestinal resection should be done.

The operation follows persistent local control and restoration or preservation of sphincter functionality in cases where tumor location is in the distal part of the rectum. To obtain local control it is necessary to perform an intestinal resection with complete dissection of the lymphatic and vascular drainage, with ligation of the vascular pedicles, and ideally dissect the planes between the mesentery and the pelvic walls or retroperitoneum.

In tumors located in the colon (cecum, ascending, transverse, descending and sigmoid), the initial approach in most patients is surgical. Even in patients with pathology

metastatic may be initiated with resection of the primary tumor.

In colon tumors, the surgical method is commonly based on the intestinal resection in which the tumor is located, with margins of 10 centimeters above and below, with a colon-anastomosiscolon, and only in selected cases such as perforation or intestinal obstruction should be placed a temporary ileostomy for right tumors or colostomy for sigmoid tumors. The surgical methods to be used will depend on where the tumor is located.

In rectal tumors, the surgical method is different depending on the location of the tumor. Generally, the length of the rectum is 15 centimeters on average above the pectinous line. Transsphincter surgery has recently been incorporated to try to maintain the anal sphincter in patients with small tumors located in the lower third of the rectum.

Postsurgical histological analysis

Usually, in almost all cases the histological diagnosis is obtained prior to the oncological procedure. For all cases in phases O-III and less than half of the cases with phases IV, initial surgery is important. Then it is essential to have the histopathological study of all the tissue resected, which will have to have all the next aspects:

- Confirm the histological type.
- Confirm the level of differentiation (good, moderate, little differentiated or undifferentiated. The

patients with low or undifferentiated adenocarcinoma have more ways of tumour recurrence and worse prognosis.

- Depth of the invasion. Number of dissected lymph nodes. A dissection of at least 12 lymph nodes is required to detect metastasised ganglia.
- Number of lymph nodes with metastases. The greater the number of nodes with metastases, the worse the prognosis. Surgical edges, independent or with presence of malignant cells. If malignant cells are present on any of the surgical edges, then there is a high risk of recurrence.
- Infiltration of malignant cells into vascular, lymphatic or perineural vessels. If it is present in some of them or all 3, there will be greater danger of recurrence.

All the above points of view will be taken into account to enter the final phase, combining the depth of invasion (T), the number of lymph nodes with metastases
(N) and with the help of expansion studies for distant metastasis sites (M). Then we must conclude the etapification: pTNM (you put the prefix p to indicate that it has been treated at the beginning with surgery)

Systemic treatment (post-radical surgery) in O-III phases

15% of patients are phase O-I, for which they do not need any additional oncological procedure, knowing that between 85 and 90% of them will be alive at 5 and 10 years. Postoperative chemotherapy (QT) does not provide any benefit.

Etapa II

Between 25 and 30% of cases will be phase II. Survival at 5 years ranges from 60% to 85% after extreme surgery, identifying a set of patients with high risk of tumor recurrence leading to cancer death. There is no agreement that such phase II patients should all receive postoperative QT (also called adjuvant QT). About 40-50% will need it, and for that it is essential to know if the patient has some of the clinical and histological components of poor prognosis.

Etapa III

30-35% of patients with colorectal cancer at the time of diagnosis will be stage III. In these cases, surgery of the primary tumor could be curative; however, 40-60% of patients will relapse and die from metastatic pathology.

The indication of adjuvant QT is basically in 100% of patients (unless there is a specific contraindication). The goals of postoperative QT is to eliminate micro-metastatic pathology, minimize local and/or distant recurrences, prolong pathological independent survival and increase universal survival (OS)

There are currently 3 adjuvant QT schemes considered as standards, both of which can be used interchangeably based on various components, such as patient's taste, availability, prices, etc.:

- FOLFOX-4: oxaliplatin, folinic acid and 5-FU, all intravenously, every 14 days for 12 cycles.
- XELOX: oxaliplatin intravenously on day 1 and capecitabine orally for 14 consecutive days with one week off, every 3 weeks for 8 cycles.
- 5-FU-folinic acid or capecitabine: once the patient is older than 70 years of age, he has comorbidities that is considered physically fragile, but he may have a vision of life greater than 2 years.

In summary, all patients with stage III colon cancer should receive adjuvant QT over 6 months with some mixture that integrates oxaliplatin (FOLFOX or XELOX). In selected cases that do not receive oxaliplatin, they should use capecitabine or 5-FULV for 6 months.

Stage IV - metastatic pathology

30-40% of patients with colorectal cancer are diagnosed in phase IV, where the primary therapeutic weapon is QT and/or white therapy, and recently immunotherapy. However, there are situations where the surgical procedure is important. In patients with liver or lung metastases, resection of the same may develop even as initial therapy, and usually followed by a systemic procedure.

Chemotherapy for metastatic disease

30-40% of patients with colorectal cancer are diagnosed in phase IV, where the primary therapeutic weapon is QT and/or white therapy, and recently immunotherapy. The advantages of the systemic procedure are:

- Improve their quality of life by reducing the magnitude of cancer-induced signs. Up to 60% of the patients have improved their symptoms, mainly in terms of weight loss, asthenia and pain and increased activity.
- Increase progression independent survival (SLP), which is the time that the patient lives with good control of signs and pathology. It could be between 7 and 9 months, which cannot be obtained without a systemic oncological procedure.
- Improve the SG. A mean survival of 18-24 months can be achieved by receiving the systemic procedure, which is considerably greater than 6-8 months without any procedure.

Active QT drugs in patients with metastatic colon and rectum cancer are: 5-FU, capecitabine, TAS 102, tegafur-uracil, S1, oxaliplatin, and irinotecan. Generally, we have the possibility to discuss the following combinations:

- May Scheme: 5-FU and folinic acid (the latter to promote the effectiveness of 5-FU).
- Capecitabine.
- FOLFOX: oxaliplatin, 5-FU and folinic acid.
- FOLFIRI: irinotecan, 5-FU and folinic acid.

- XELOX: capecitabine and oxaliplatin.
- XELIRI: capecitabine and irinotecan.
- FOLFOXIRI: oxaliplatin, irinotecan, 5-FU and folinic acid.

White therapy for metastatic pathology

Progress in reasoning the different molecular mechanisms involved in cancer allowed the development of molecular targets. Different tactics have been used to generate therapeutic targets, with angiogenesis and EGFR being the most studied in advanced colorectal cancer.

Anti angiogenesis

Angiogenesis (formation of new blood vessels) was important in tumor growth and spread. There are several related components, being the vascular endothelium growth component (VEGF) fundamental in tumor development. VEGF is a glycoprotein with different isoforms (VEGF-A, VEGF-B, VEGF-C and VEGF-D) bound by two tyrosine kinase receptors called VEGFR-1 and VEGFR-2. The binding of VEGF isoform to both receptors causes activation of the cell signaling cascade, with neovascularization, mitogenesis and elimination of apoptosis. There are currently 3 available antiangiogenic drugs for use in metastatic colorectal cancer: bevacizumab, ramucirumab and aflibercept.

These drugs are generally well tolerated, with controllable adverse effects. Among the most important of this set are hypertension

arterial, thromboembolic events and proteinuria. There is no biomarker that can predict the response to this antineoplastic therapy.

Anti-receptor therapy of the epidermal augmentation component

The epidermal increment element (EGF) is an EGFR ligand in the tyrosine kinase receptor family (ErbB). After the alliance of EGF to EGFR, it triggers an intracellular signaling cascade stimulating tumor growth and progression. To counteract this signaling pathway, we have 2 monoclonal antibodies: cetuximab and panitumumab, a humanized monoclonal antibody that binds selectively to EGFR inhibiting intracellular signaling and thus angiogenesis and metastasis.

There are currently biomarkers determined in tumor tissue to establish sensitivity to these antibodies: they are the oncogenes KRAS and NRAS in the wild state (wild type [WT]), which are unmutated in about 50% of patients with colorectal cancer

Given the existence of metastatic colorectal cancer, mutations in RAS and BRAF as well as MSI must be determined. In first-line regimens QT should generally be considered in conjunction with a monoclonal antibody.

Immunotherapy

In cancer patients the cytotoxic immune response may be deregulated, which can influence the host. Its functionality can be restored by blocking the receptor or its ligands. This line of procedure, recently accepted by the Food and Drug Administration in patients with multitreated metastatic colorectal cancer, is indicated exclusively in patients who have a response marker, the MSI (test developed by immunohistochemistry or by polymerase chain attitude) or error-repairing gene deficiency, which will be present in 5-8% of cases. Pembrolizumab and nivolumab are available, which in initial studies have been shown to be fundamental for mean survival.

MONITORING AND FOLLOW-UP

After completion of the multidisciplinary oncological procedure, a follow-up program based on medical evaluation with interrogation and physical investigation every 3 months for the first 2 years (then every 6 months), ACE tumor marker taken every 36 months, computed tomography of the abdomen and pelvis every year and colonoscopy every 2 years, all mentioned during the first 5 years. It will later be possible to spread the evaluations every 2-3 years.

EARLY DETECTION

In a population with dangerous components due to their clinical conditions such as obesity, sedentary lifestyle,

diabetes mellitus, metabolic syndrome or diet rich in fats, it is advised at least to develop decision based on blood hidden in feces, in age of more than 40 years. If there are other related precedents, it is imperative to do colonoscopy at an early age and the specific genetic mutational test to be positive in the family member with colon or rectal cancer.

REFERENCE:

FANDIÑO, Q. M. (2009 ISBN: 84-669-2813-8). IMPACTO PRONÓSTICO DE LAS CÉLULAS TUMORALES RESIDUALES AISLADAS EN SANGRE PERIFÉRICA EN CÁNCER DE MAMA DE ALTO RIESGO. Recuperado el 24 de ABRIL de 2015, de UNIVERSIDAD COMPLUTENSE DE MADRID: http://biblioteca.ucm.es/tesis/med/ucm-t28663.pdf

Marie, K. F. (2010). Cáncer de mama en México: una prioridad apremiante. Recuperado el 24 de abril de 2015, de SCIELO: http://www.scielo.org.mx/scielo.php?pid=S0036-36342009000800026&script=sci_arttext&tlng=en

MSP ARGENTINA, M. D. (2012). ESTADISTICAS INCIDENCIA DE CANCER. Recuperado el 24 de ABRIL de 2015, de INSTITUTO NACIONAL DEL CANCER: http://www.msal.gob.ar/inc/index.php/acercadel-cancer/estadisticas

Thomas T, Althouse A, Sigler L, Arnold R, Chu E, White DB, et al. Stronger therapeutic alliance is associated with better quality

of life among patients with advanced cancer. Psychooncology. 2021 Jul 8;30(7):1086–94