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REVIEW ARTICLE

Cutaneous melanoma as one of the most serious neoplasms facing medicine

El melanoma cutáneo como una de las neoplasias más graves que enfrenta la medicina

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ABSTRACT

Introduction: melanoma is a skin cancer that originates in melanocytes and is the third most common skin neoplasm. It mainly affects people between the fifth and sixth decades of life, although its incidence in people between 25 and 29 years of age has increased.

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Objective: to describe the most important aspects related to cutaneous melanoma.

Methods: an integrative literature review on cutaneous melanoma was carried out, using articles in Spanish and English from the last five years. Duplicates and those of low scientific quality were excluded 26 references of the 34 consulted were used. The review provides an updated and comprehensive overview of the state of knowledge on cutaneous melanoma, highlighting the importance of recent research in this field.

Development: melanoma is a type of skin cancer whose incidence has increased in recent years, especially in middle-aged men with occupational exposure to ultraviolet rays. There are four main types of melanoma and its most common type of spread is superficial. Risk factors include a family or personal history of melanoma, multiple atypical moles, and a weakened immune system.

Conclusions: cutaneous melanoma is difficult to cure in advanced stages, but early diagnosis can contribute to a possible cure. Clinical knowledge and risk factors, added to adequate treatment, can increase patient survival.

Keywords: Skin cancer; Cutaneous neoplasms; Melanocytes

RESUMEN

Introducción: el melanoma es un cáncer cutáneo que se origina en los melanocitos y es la tercera neoplasia más frecuente en la piel. Afecta principalmente a personas entre la quinta y sexta década de vida, aunque su incidencia en personas de entre 25 y 29 años se ha incrementado.

Objetivo: describir los aspectos más importantes relacionados con el melanoma cutáneo.

Métodos: se realizó una revisión bibliográfica integradora sobre el melanoma cutáneo, utilizando artículos en español e inglés de los últimos cinco años. Se excluyeron los duplicados y aquellos de baja calidad científica. Se utilizaron 26 referencias de las 34 consultadas. La revisión proporciona una visión actualizada y completa del estado del conocimiento sobre el melanoma cutáneo, destacando la importancia de la investigación reciente en este campo.

MedEst. 2024; Vol.4 No.3
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Desarrollo: el melanoma es un tipo de cáncer de piel cuya incidencia ha aumentado en los últimos años, especialmente en hombres de mediana edad con exposición ocupacional a los rayos ultravioletas. Existen cuatro tipos principales de melanoma y su tipo de propagación más común es la superficial. Los factores de riesgo incluyen antecedentes familiares o personales de melanoma, múltiples lunares atípicos y un sistema inmunológico debilitado.

Conclusiones: el melanoma cutáneo es difícil de curar en etapas avanzadas, pero el diagnóstico temprano puede contribuir a una posible cura. El conocimiento clínico y de los los factores de riesgo, sumado a un tratamiento adecuado, pueden aumentar la supervivencia de los pacientes.

Palabras clave: Cáncer de piel; Enfermedades de la piel; Neoplasias cutáneas

INTRODUCTION

Melanoma is a form of skin cancer that begins in melanocytes, the cells that produce melanin, the pigment that gives color to skin and hair. It can appear on the skin, in moles, on mucous membranes, or in any area that contains melanocytes, such as the oral cavity, eyes, anus, or genitals. (1)

Skin melanoma is the third most common type of skin cancer and has the greatest impact on mortality. Of multifactorial etiology, its prevalence has been reported to have increased for approximately two decades. It ranks seventh in frequency among all tumors. 80 % of cases are locally advanced. (2)

According to the World Health Organization (WHO), melanoma accounts for about 1 % of all cancers diagnosed worldwide. The incidence of melanoma is increasing globally, with an estimated annual growth of 3 %. Although the five-year survival rate for early-stage melanoma is high, the disease can be fatal if not diagnosed and treated early. The WHO estimates that approximately 232 000 people die from melanoma each year. (2)

The increase in incidence is largely attributed to increased exposure to ultraviolet (UV) radiation due to lifestyle changes such as increased outdoor activities and use of tanning beds. The global distribution of melanoma is not uniform. Countries with the highest incidence rates are in Australia, New Zealand, Northern Europe, and the United States, while other regions such as Africa and Asia have lower incidence rates. (2)

MedEst. 2024; Vol.4 No.3
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Of the three types of skin cancer caused by chronic and excessive sun exposure (basal cell carcinoma, squamous cell carcinoma, and malignant melanoma), basal cell carcinoma is the most common. However, melanoma is the most invasive and dangerous type. (3)

Regarding its history, it is important to note that its name comes from the Greek words melas (black) and oma (tumor), and is used to name the malignant transformation of the skin pigment cells: melanocytes. In general, it is a very invasive tumor due to its ability to generate metastasis. (4)

Although melanoma occurs most frequently between the fifth and sixth decades of life, the incidence among people aged 25 to 29 has increased and has become the most common cancer in this age group. Of those affected, 95 % of cases originate in the skin and the remaining 5 % in the eyes and mucous membranes (mouth, vagina or anus). Similarly, between 3 and 10 % of cases present as metastatic disease, without a clinically apparent primary lesion. Today, it is considered the fifth most common malignancy in men and the sixth in women, associated with high morbidity and mortality, due to the risk of metastasis in the regional lymph nodes of the affected area and distant areas. (5)

Treatment recommendations depend on many factors, including the thickness of the primary melanoma, the risk of cancer spreading, the stage of the melanoma and the presence of specific genetic changes in its cells, its growth rate, and other patient factors. (1,2)

Considering that cutaneous melanoma is a serious form of cancer that can be fatal if not detected early, the aim of the present research is to describe the most important aspects related to cutaneous melanoma, specifically its diagnosis and treatment.

MATERIALS AND METHODS

An integrative bibliographic review of the literature on cutaneous melanoma was conducted. This facilitated the formulation of global conclusions based on the research analyzed. The following were taken into account for its implementation: identification of the topic and formulation of the guiding question, literature search, definition of information to be extracted from the selected studies, critical analysis of the included research and synthesis of knowledge. This literature review consisted of a search in SciELO, Google Scholar and PubMed. The search tags used were: Skin cancer; Skin diseases; Skin neoplasms.

MedEst. 2024; Vol.4 No.3
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The selection criteria were: articles with free access to the full text, published in Spanish and English. Duplicates and those with low scientific quality were excluded, evaluated through critical reading. 26 references were used out of the 34 consulted, of which the majority of these are from the last five years and in English and Spanish.

DEVELOPMENT

Epidemiology

The incidence of melanoma varies depending on latitude, gender and skin phenotype, but it is clear that it has been increasing exponentially in recent years. The most frequent presentation is in middle-aged patients, around 40-50 years, with a higher prevalence in men due to their greater exposure to ultraviolet rays (probably of occupational origin). Although cutaneous melanoma represents only 3 % of all types of skin cancer, it remains the main cause of death today. (6)

Types of melanoma

There are four main types of melanoma and a few minor subtypes:

1) Superficial spreading melanoma: accounts for 70 % of all melanomas. It appears as a plaque with brownish or dark, raised, irregular, indurated areas, often showing red, white, black, or blue spots, or sometimes raised nodules. Small indentations or irregularities may be seen along the edges, with enlargement or color changes. On histological examination, atypical melanocytes characteristically invade the dermis and epidermis. (7)

2) Nodular melanoma: This type accounts for approximately 15 % of melanomas. It often appears rapidly as a lump on the skin. It is usually black, but may be pink or red. (8)

It can appear anywhere on the body and appears as a dark, raised papule or plaque, varying in color from pearly gray to black. Sometimes the lesion contains little pigment or may resemble a vascular tumor. Unless ulcerated, nodular melanoma is asymptomatic, although patients often seek medical attention because the lesion enlarges rapidly. (9)

3) Lentigo maligna melanoma: In the case of this type of lesion, the procedure to follow is to take a biopsy to confirm the diagnosis. However, the appropriate method for the biopsy is a challenge, since the lesions usually have poorly

MedEst. 2024; Vol.4 No.3
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defined borders and are large for an aesthetically very sensitive area such as the face. (9)

According to the guidelines for the management of melanoma, the most appropriate method for taking a biopsy is the excisional sample, while the incisional or shave biopsy is usually suboptimal. However, an acceptable option is to perform a deep incisional or punch biopsy of the area that clinically appears deeper. (9)

4) Lentiginous acral melanoma: in early stages, it is diagnosed less frequently than lentigo maligna melanoma and superficial spreading melanoma.

This fact could be explained by several non-mutually exclusive hypotheses:

a) A more aggressive biological behavior than in other types of malignant melanoma.

b) Lack of awareness in the population of the possibility of melanoma occurring in the subungual or palmoplantar regions.

c) Clinical presentation different from other types of malignant melanoma.

d) Difficulty in detecting lesions because they are hidden from view during daily life or due to less primary health care due to the age group in which they occur. (10)

Stage classification of cutaneous melanoma: (11)

Stage 0: Abnormal cells are found only in the outer layer of the skin, without invading deeper tissues.

Stage I: Cancer is found in the epidermis or beginning of the dermis. The thickness of the tumor is less than 1-2 mm.

Stage II: Cancer affects the dermis. The thickness is between 2 mm and 4 mm.

Stage III: Tumor is greater than 4 mm thick or affects tissues below the skin. Presence of satellite tumors around the main lesion or involvement of lymph nodes near the main lesion.

Stage IV: Tumor affects organs or lymph nodes far from the original tumor.

MedEst. 2024; Vol.4 No.3
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Risk factors

The main risk factors for developing cutaneous melanoma depend on the host, such as family or personal history of melanoma and the presence of multiple atypical nevi. The patient's genetic susceptibility has been found to be very important.

Between 25 and 40 % of families with a history of multiple cases of melanoma have alterations in the cyclin-dependent kinase inhibitor 2A (CDKN2A) or in the gene that codes for cyclin-dependent kinase 4 (CDK4) - tumor suppressor genes - and also alterations in the p53 protein. The immunological status (in patients with transplants the risk increases approximately 100 times), sun sensitivity and exposure to ultraviolet rays are additional factors of great importance. (12)

Exposure to ultraviolet radiation from the Sun plays an important role in the development of skin cancer. People who live in high places or in areas with sunlight throughout the year have a higher risk of developing skin cancer. People who spend a lot of time outdoors in the afternoon are also at risk. Recreational outdoor tanning should be avoided to reduce the risk of skin cancer. (13)

Although melanoma appears to be most directly linked to exposure to solar ultraviolet B (UVB) radiation, new information suggests that ultraviolet A (UVA) radiation may also affect the development of melanoma and skin cancer, basal cell carcinoma, and squamous cell carcinoma. While UVB radiation causes sunburn and does not penetrate car windows or other types of glass, UVA radiation can pass through glass and cause skin aging, wrinkles, and skin cancer. Therefore, it is important to protect the skin from both UVA and UVB radiation. (13)

People with a weakened immune system (due to certain medical conditions or treatments) are more likely to develop several types of skin cancer, including melanoma. For example, organ transplant recipients are often given medications that weaken the immune system to prevent rejection of the new organ. This increases your risk of developing melanoma. People infected with HIV, the virus that causes AIDS, often have a weakened immune system and an increased risk of developing melanoma. (11)

Heredity is the most important non-modifiable risk factor for melanoma. 8-12 % of patients with cutaneous melanoma have a family history of the disease.

MedEst. 2024; Vol.4 No.3
ISSN: 2789-7567 RNPS: 2524

For example, parents with melanoma represent a relative risk of up to 2,40 % for their children. There are genetic syndromes that predispose patients to melanoma, such as carrying the BRCA2 gene (the same gene involved in the development of breast and ovarian cancer). In addition, 1 in 5 people with xeroderma pigmentosum will develop cutaneous melanoma in their lifetime. (14)

Other factors can contribute to the risk of cancer spreading (metastasis), such as when open sores (ulcers) are observed under a microscope on the skin in the area, or the number of cancer cells dividing (mitosis).

Diagnosis of cutaneous melanomas

Although melanoma can spread rapidly and cause death within a few months of detection, the 5-year cure rate for superficial lesions diagnosed early is very high. Therefore, cure depends on early diagnosis and treatment. For tumors of cutaneous origin (non-subungual and non-central nervous system melanomas) that have not metastasized, the survival rate varies depending on the thickness of the tumor at diagnosis. (16)

The 5-year survival rate ranges from 97 % for patients with stage IA melanoma to 53 % for patients with stage IIC melanoma. The 10-year survival rate ranges from 93 % for patients with stage IA melanoma to 39 % for patients with stage IIC melanoma. (7)

The degree of lymphocytic infiltration, which represents the reaction of the patient's immune system, can be correlated with the level of invasion and prognosis. The chances of cure are greatest when lymphocytic infiltration is limited to the most superficial lesions, and decrease at deeper levels of tumor cell invasion, ulceration, and vascular or lymphatic invasion. (9)

As with all neoplasias, the prognosis depends on the stage. At admission, 85 % of patients have local disease, 13 % local disease with lymph node metastasis, and only 5 % distant metastasis. However, survival varies greatly between patients of the same stage due to tumor-specific prognostic and histological factors. Perhaps most important is the level of intrusion or Breslow level. (17)

Breslow should be assessable with an adequate biopsy. This is because the advanced tests required, the final surgical margin, and the patient's prognosis depend on it. Breslow is the depth that a melanoma reaches, measured in millimeters from the most superficial layer of the epidermis to the point of

MedEst. 2024; Vol.4 No.3
ISSN: 2789-7567 RNPS: 2524

maximum penetration. The higher the Breslow, the worse the patient's prognosis and the lower the cure rate. (18)

In general, patients with localized disease and tumors less than 1 mm thick have a good prognosis, with a 5-year survival rate of 90 %. The survival rate is 50 % for tumors greater than 1 mm thick and decreases to 20 % for lymph node metastases. (19)

For patients with distant metastases, the 5-year survival rate rarely exceeds 10 %, but the prognosis may be better depending on the site of the metastasis. Patients with subcutaneous tissue metastases (M1A) usually achieve an adequate survival and disease progression can be greatly delayed. (20)

Excisional biopsy is not appropriate in: palms, soles, face, fingers, subungual region, auricle, or very large lesions; In these cases, the indication for an incisional biopsy is accepted, taking the portion that clinically proves to be deeper. In the event that the incisional biopsy does not allow an accurate microstaging of the patient, which is frequent due to an underestimation of the thickness of the lesion, it is appropriate to repeat the procedure, and preferably proceed with an excisional biopsy. (21)

Current guidelines for cutaneous melanoma recommend, once the diagnosis has been confirmed by the anatomopathological study, the removal with safety margins of the primary tumor and the performance of a selective biopsy of the sentinel lymph node (SLNB), based on the Breslow thickness. SLNB is a prognostic and therapeutic procedure with fewer complications than elective lymph node dissection (preventive or prophylactic lymph node dissection of the supposed lymphatic drainage area, which until now was performed on all patients with cutaneous melanoma). (22)

SLNB is based on the hypothesis that lymphatic metastases follow an orderly, sequential, and non-random progression. Therefore, examination of the sentinel node, the first lymphatic drainage station, reliably reflects the status of the remaining regional lymph nodes. (23)

This is a useful method to detect potential nodular metastasis and prevent unnecessary lymphadenectomy in patients without lymph node involvement.

Treatments

Local therapy

MedEst. 2024; Vol.4 No.3
ISSN: 2789-7567 RNPS: 2524

If melanoma is confirmed, the tumor or tumor area should be completely removed. Narrow (1 to 2 cm) versus wide (> 3 cm) resections consistently show similar rates of local and disease-free recurrence, as well as overall survival. Wide margins are no longer recommended—exact cutoffs have not been specified—but general recommendations are: Breslow melanoma less than 1 mm thick, the recommended cutoff is 1 cm. For melanomas greater than 1 mm Breslow thickness, a 2 cm margin is recommended. (24)

Immunotherapy is a drug therapy that helps the immune system fight cancer. The body's immune system may not attack cancer because cancer cells produce proteins that blind immune cells. (25)

Immunotherapy works because it interrupts this process, and is often recommended after surgery for melanoma that has spread to lymph nodes or other parts of the body. If the melanoma cannot be completely removed, immunotherapy drugs may be injected. (25)

Chemotherapy

Chemotherapy is the use of drugs that destroy cancer cells, usually by stopping them from growing, dividing, and making new cells. Traditional types of chemotherapy are still used to treat melanoma, but they are usually no longer used as a first-line treatment. (26)

A chemotherapy regimen or schedule consists of a specific number of cycles, usually given over a period of time. The patient may receive one drug at a time or a combination of several drugs given at the same time. Dacarbazine (DTIC, available as a generic drug) is the only chemotherapy drug approved by the Food and Drug Administration (FDA) for the treatment of melanoma. (12)

Temozolomide (Temodar) is an oral version of dacarbazine and is used to treat stage IV melanoma. Side effects of chemotherapy depend on the patient and the dose used, but may include fatigue, risk of infection, nausea and vomiting, nail changes, loss of appetite, diarrhea, nerve damage causing sensory changes, and associated hair loss. These side effects usually disappear once treatment is completed. (12)

CONCLUSIONS

MedEst. 2024; Vol.4 No.3
ISSN: 2789-7567 RNPS: 2524

Understanding the causes, development and spread of melanoma is crucial for prevention and early detection. Research aims to identify cancer in its early stages, facilitating treatment and recovery. Early detection is vital to saving lives, as treatment is less invasive. Advanced therapies are being investigated to improve the quality of life of patients.

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STATEMENT OF AUTHORSHIP

MOCM: Conceptualization, Data curation, Formal analysis, Investigation, Project administration, Resources, Validation, Writing the original draft.

LHC: Conceptualization, Investigation, Methodology, Project administration, Resources, Validation and Writing, review and editing.

NPR: Conceptualization, Investigation, Methodology, Project administration, Resources, Validation and Writing, review and editing.

CONFLICT OF INTEREST

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