

Nodular Malignant Melanoma

Jiménez-Báez María Valeria¹, Cachón-Santana Cindy Margarita², Rodríguez-Cruz Andrea Elizabeth², Milla-González Ludivina³, Luis Sandoval Jurado¹, María Margarita Chavez Hernandez¹, Enrique Leobardo Ureña Bogarín¹

¹Department of Medical Services, Mexican Social Security Institute, Delegation in Quintana Roo, Clinical Research Group of IMSS in Quintana Roo (GRICIQ), Mexico, ²Health Sciences Division, University of Quintana Roo, Mexico General Hospital Clinical Cycles No. 17, Mexican Institute of Social Security, Cancun, Quintana Roo, México, ³Department of Internal Medicine, Mexican Social Security Institute (IMSS), Medical Dermatologist of IMSS Cancún, Mexico

ABSTRACT

Malignant melanoma is one of the most aggressive neoplasms of the skin. It originates from the melanocytes, which are cells derived embryologically from the neural crest and migrate to the epidermal basal layer. It is characterized by producing pigmentation as well as being susceptible to metastasis. We report the case of a 36-year-old female patient with advanced clinical stage and distant commitment. The biopsy confirmed the presence of Grade III invasive nodular cutaneous melanoma in the left subscapular region with lymph node metastasis with reactive hyperplasia. An exploratory research is carried out with the bibliographic review in scientific journals with evidence level II–IV. In portals PubMed, Redalyc, BVS, and UpToDate. 81241 met criteria 2248 of which 629 were chosen for having access to the full text and of these 496 are more current (as of 2008), and in the end, 27 articles were selected that met all the inclusion criteria to this article. Due to the increase in the incidence of this disease in recent years and its poor prognosis in short to medium term, it is important to know and follow-up on patients with known risk factors for this disease such as the presence of previous nevi, with emphasis on measures of prevention.

Key words: Metastasis, nodular malignant melanoma, skin

INTRODUCTION

Malignant melanoma is one of the most aggressive neoplasms of the skin. It originates from the melanocytes, which are cells derived from the neural crest to end up in the epidermal basal layer forming the melanic-epidermal unit where melanocytes and keratinocytes have a proportionality of 1/36.2. It is characterized by producing pigmentation as well as being susceptible to metastasis.^[1,2]

It frequently occurs in four clinical varieties according to Clark *et al.* and McGovern: (1) Surface extension melanoma, (2) lentigo malignant melanoma, (3) nodular melanoma, and (4) lentiginous acral melanoma. There are some other less common clinical varieties such as mucosal and paramucosal melanoma. It is a multifactorial disease

where the predisposing factor is intense exposure to ultraviolet (UV) rays and Caucasian race.^[3,4]

The factors that increase the possibility of suffering a malignant melanoma are family history of melanoma (regardless of type or location), personal history of some type of cancer, large congenital nevi, high number of acquired nevi or atypical pigmented lesions, and genetic predisposition for mutations in CDKN2A and CDK4.^[5]

In the world the incidence of skin cancer has been increasing, every year 2–3 million cases of non-melanoma skin cancer and 132,000 cases of melanoma. One in three patients diagnosed with cancer has skin cancer.^[3,4]

Cutaneous melanoma represents 4% of malignant tumors of the skin, and its survival depends on the extent of the

Address for correspondence:

Jiménez-Báez María Valeria, Jefatura de Servicios Prestaciones Médicos Av. Politécnico Nacional S/N SMZ 509, CP. 77533 Cancún, Quintana Roo, Mexico. E-mail: valeria.jimenezb@gmail.com

© 2019 The Author(s). This open access article is distributed under a Creative Commons Attribution (CC-BY) 4.0 license.

disease.^[6,7] The most common clinical variant of malignant melanoma in the world is a superficial extension (60–70% of cases) followed by nodular melanoma (15–30%) and acral lentiginous melanoma (5–10%).^[5,6]

In Latin America, the International Agency for Research on Cancer estimates a frequency of presentation of 2 per 100,000 inhabitants. In Mexico, melanoma ranks tenth in all neoplasms and third in skin cancer with 14.1%.^[8]

It is one of the most common neoplasms in the young adult, with predominance in the female sex during the three decades of life.^[6]

The presentation in men is in the trunk and women, it is in the lower extremities.^[3]

Its incidence has increased in recent years around the world, having a higher peak in tropical countries because they are exposed to the sun since childhood, the lack of habit by not using sunscreen, and the greater diagnosis by the dermatoscope that allows detecting early lesions.^[9]

Melanoma ranks third with 7.9% in Mexico and is the cause of 75% of deaths from skin cancer.^[10] In Mexico, the true incidence of malignant melanoma is unknown;^[11] however, in 2012 the Dermatological Center of Yucatan found 177 patients with skin cancer, where melanoma had a prevalence of 1.7%.^[12] The purpose of this work is to report a case of malignant nodular malignant melanoma, with an apparent spontaneous regression, whose personal ignorance of the patient for attention to the presence of spots or moles and the doctor of opportunity for the appropriate derivation, led to an injury invasive.

CASE REPORT

This is a 33-year-old female patient, originally from Holpelchen, Campeche and residing in Cancún, Quintana Roo, referred to primary health-care medical unit with a diagnosis of Nevo Melanocítico, who goes to the dermatology service for presenting dermatosis located in the left infrascapular region, constituted by neoformation formed by two exophytic lesions with 4 cm, hyperchromic macula with an exophytic center and heterochromia of three variations color, hypochromic with pink tint, dark brown and bluish black, with perilesional achromic halo and palpation with induration, mobile and painful and not adhered to deep planes [Figure 1]. He began his condition 5 years ago with a small nevus, which has been adding occasional bleeding and pain for 3 years, with progressive growth to the present date. He mentions faster growth after his last pregnancy.

An excisional biopsy of the lesion was performed in the dermatology department where an asymmetric proliferation of atypical epithelioid and spindle-shaped melanocytes was observed, individually and confluently arranged in



Figure 1: Neoformation consisting of two exophytic lesions on a hyperchromic macula with an exophytic center and heterochromia of the color of three variations, hypochromic with pink tint, dark brown, and bluish black, with acromic halo perilesion

discohesive nests and mantles that invade the nerve fibers, and the muscle tissue present in the cut. The melanocytes are large, pleomorphic with pale cytoplasm, eosinophilic with melanic pigment in their interior. The nuclei are of irregular, hyperchromatic, and pleomorphic contours, some of them show individual cell necrosis.

Given the histopathology result, a secondary intervention was performed 14 days after the first one for the widening of margins and left axillary dissection. The histopathological report of the piece showed 3 mitoses/mm². In the papillary dermis and superficial reticular lymphocyte inflammatory infiltrate that surrounds and infiltrates the neoformation, there is a fall of pigment with melanophages and cytoid bodies. Residual axillary conglomerate with melanoma metastasis, nine ganglia with reactive hyperplasia.

The final histopathological report details a Grade III invasive nodular cutaneous melanoma of at least 12 mm thickness on the Breslow, Clark level V scale of the skin of the left subscapular region.

It is sent to the oncology service 2 days after the second intervention where a computerized axial tomography (CT) is indicated that reported asymmetric breasts in size, cystic lesion of the right ovary 21 mm × 17 mm suggestive of metastasis. As prophylaxis against a possible invasion of the central nervous system, it was indicated to initiate radiotherapy and pegylated interferon and ipilimumab as adjuvant therapy.

DISCUSSION

Nodular malignant melanoma is a tumor that affects people of any age, especially young adults.^[13] The main risk factor is exposure

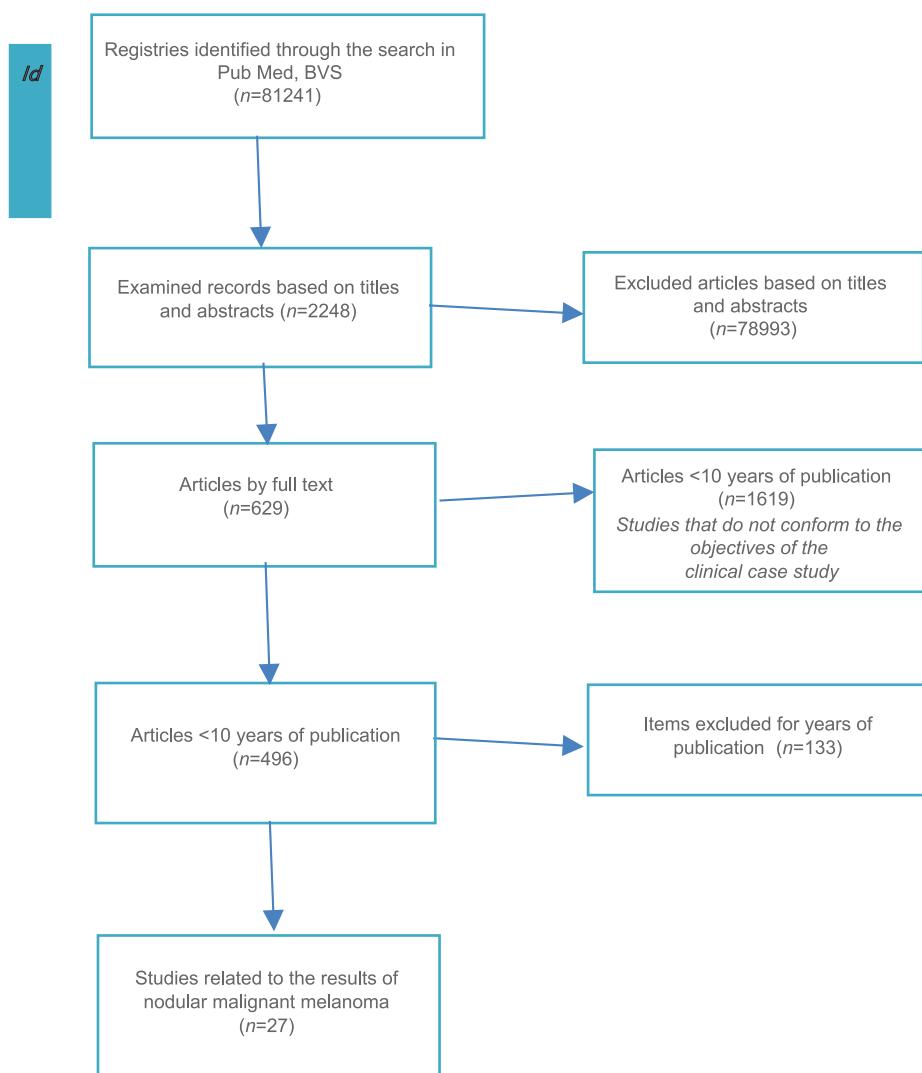


Chart 1: Studies related to the results of nodular malignant melanoma

to sunlight, which produces variations in DNA and its suppression of cellular apoptosis bound to skin phototype I and II.^[14] It appears mainly in the trunk and extremities, presenting initially and exclusively vertical growth phase, conditioning aggressive behavior, and worse prognosis.^[14] This type of melanoma has an orientation to lymphatic and hematic dissemination, and up to 4% of cases it is discovered by metastasis.^[15]

In this case, the location of the tumor was found in a protected photo area in the subscapular region, characteristic of this variant of melanoma and skin phototype III, as well as metastases to lymph nodes.

In most patients, the disease is detected when localized and can be cured by excising the primary tumor *in situ*; however, many patients are diagnosed in the metastatic phase. The 10-year survival rate with metastasis is <10%.^[8] The delay in the diagnosis of malignant melanoma is common in the

pediatric population and can be attributed to the atypical presentation, although on other occasions it is due to the reluctance to consider the condition.^[9] It is fundamental, therefore, to apply the ABCDE criteria with the help of dermatoscopy and biopsy in highly suggestive cases.^[9,10]

As for the clinic, it depends fundamentally on its growth pattern; the majority is initially presented with a phase of radial growth (intraepidermal) and later a vertical growth consisting of a growth toward the dermis leading to the vicinity of vascular and lymphatic structures causing or increasing the chances of metastasis, a situation that occurred in our case where the radial phase was minimal, and the vertical phase was the one that prevailed leading to a darker prognosis. In a study conducted by Calderón *et al.* in 2017, they found nRAS mutations in 28%, as well as their mean evolution time was 7.79 years.^[16-18] In the case of our patient, she had a diagnostic delay of 4.5 years.

Table 1: Summary Table of included studies

No.	Reference	Methods	Results	Conclusions
1	Melanoma cutáneo ^[1]	Review	Review	Cutaneous melanoma is the most malignant tumor of the skin and has a great capacity to metastasize. Even when some risk factors are known, diagnosis and early treatment are the only strategies that have been shown to improve the prognosis of those who suffer from it, and its management is a challenge
2	Estudio epidemiológico de melanoma maligno en el American British Cowdry Medical Center ^[2]	Retrospective, descriptive, and linear study	123 histopathological reports were included, corresponding to 63 male patients and 60 female patients. The age ranged between 19 and 97 years. 73 cases were primary, of them 61, of skin and 12, extracutaneous, 50 were metastases; 30 in lymph nodes and 20 extranodal. The predominant Clark level was III, and Breslow II. 57 cases were HMB45 and 50 positive to S100	The frequency of this neoplasm attracts attention in comparison with other groups, as well as the number of extracutaneous malignant melanomas and the number of extranodal metastases. We consider an important contribution to an epidemiological study that should be carried out at the national level
3	Epidemiología del cáncer de piel en pacientes de la Clínica de Dermatología del Centro Dermatológico Dr. Ladislao de la Pascua. Estudio retrospectivo de los últimos ocho años ^[3]	Descriptive and retrospective study cases and controls	We reviewed 2185 records with 4743 histopathologically confirmed lesions. The most common cutaneous neoplasm was basal cell carcinoma, with a prevalence of 74% (with predominance of the clinical tumor and superficial variety, respectively), followed by epidermoid carcinoma with 14% (nodular keratotic type and Bowen's disease) and malignant melanoma with 3% (nodular variety and lentiginous acral). We also found: Sarcomas, cutaneous lymphomas and dermatofibroma sproptuberans. Basal cell and epidermoid carcinomas predominated in the seventh decade of life (26 and 24%, respectively), malignant melanoma was observed in the sixth decade (20%) and the rest of the neoplasms in the fifth decade. The most common varieties in the histopathological findings were: Solid basal cell carcinoma,	The results of this study coincide with that reported in the international bibliography, except for the higher frequency of neoplasms in women. We agree with the information that is reported in our country

(Contd...)

Table 1: (Continued)

4	Prevalencia del cáncer de piel en tres ciudades de México ^[5]	<p>Retrospective, descriptive and linear study Frequency was studied by gender, age, topography, affected organ, Clark and Breslow levels, studies with immunohistochemistry and metastases</p>	<p>We examined 443 subjects in which eight cases of skin cancer were documented, seven in women and one in men, of which six correspond to basal cell carcinoma and two to malignant melanoma, three of these in patients with prototype II, two with prototype III and three with prototype IV. 75% of patients diagnosed with skin cancer had no history of premalignant lesions, however, analyzing the suspicious lesions found a significant relationship between the presence of cancer and these lesions, with an increased risk of 3.4 times</p>	<p>The sample size was small, with heterogeneous population groups, so the results are not comparable to what happens in other states of the country</p>	<p>Skin cancer was one of the main reasons for consultation at the Centro Dermatológico de Yucatán in 2012. It was more frequent in Yucatecan women in the seventh decade of life. Pediatric cases and multiple skin cancer were described *More studies are required to know the real effect of the disease</p>
5	Epidemiología del cáncer de piel en el Centro Dermatológico de Yucatán durante 2012 ^[6]	<p>Retrospective, descriptive and observational study. All patients diagnosed with skin cancer confirmed with the histopathological study. The analysis of the data was carried out with descriptive statistics, calculation of proportions and measures of central tendency</p>	<p>We found 177 patients with skin cancer. The prevalence was 1.7%, 39% men and 61% women. The average age was 63.7 years. 53.6% were engaged in housework. 93.8% came from Yucatan. The most frequent tumor was basal cell (77%), followed by spinocellular (21%) and melanoma (2%). The most affected region was the face (74.2%). There were 28 patients with multiple skin cancer. The average time of evolution was 31 months</p>	<p>The frequency of melanoma showed variable increase in each registered year. A higher proportion of affected women was found, the average age of the population was 62.62 years. The most frequent subtype was lentiginous acral melanoma, followed by nodular melanoma. Subungual melanoma</p>	<p>(Contd...)</p>
6	Melanoma cutáneo: 12 años de experiencia ^[7]	<p>Retrospective, observational, descriptive and transversal study. We reviewed the files of patients of the Dermatology and Dermato-oncology Department of the General Hospital of Mexico with a registered diagnosis of histopathologically proven</p>	<p>We included 195 cases of cutaneous melanoma confirmed with the histopathological report, of these 19 cases with incomplete file were excluded. 176 cases were obtained, of which 57 (32%) were men. Lentiginous sacral melanoma affected 105 cases (60%), followed by nodular melanoma with 36 cases (20%), lentigo malignant</p>	<p>The frequency of melanoma showed variable increase in each registered year. A higher proportion of affected women was found, the average age of the population was 62.62 years. The most frequent subtype was lentiginous acral melanoma, followed by nodular melanoma. Subungual melanoma</p>	<p>(Contd...)</p>

Table 1: (Continued)

cutaneous melanoma, attended from January 1, 2003, to December 31, 2014. The statistical analysis was carried out descriptively through the program SPSS v 20.0	Review		melanoma in 23 cases (13%) and superficial extension melanoma in 12 cases (7%). Subgroup analysis was performed for each subtype of melanoma	Have a vision of genetics of melanomas from their cells of origin through different types of precursor lesions will allow us to achieve an improved diagnosis, early recognition of lesions that have a higher risk of progression and to be able to intervene in early stages of cancer. The gold standard to evaluate the malignant potential of melanocytic neoplasms is the histopathology (biopsy). Biomarkers are expected to help us define the progression of the lesions individually and are expected to play an increasingly important role in helping the diagnostic classification.	The influence of UV radiation on the development and evolution of melanomas in Caucasians requires that public health campaigns be disseminated to avoid excessive exposure to the sun
From melanocyte to melanoma ^[8]		Review			
Melanoma. Fundamentos del diagnóstico y la terapéutica ^[9]		Review			
Comportamiento del cáncer de piel en Güines y San José de las Lajas ^[10]		Review			(Contd...)

Table 1: (Continued)

10	Valoración inicial, diagnóstico, estadificación, tratamiento y seguimiento de los pacientes con melanoma maligno primario de piel. Documento de consenso de la "Xarxa de Centres de Melanoma de Catalunya i Balears" ^[11]	Consensus document	The knowledge and diagnosis of melanoma are of utmost importance since it is wrongly underestimated with respect to other types of cancer.
11	Melanoma: Patogénesis, clínica e histopatología ^[12]	Review article	The main genes recognized in melanoma are CDKN2A and CDK4, involved in the control of the cell cycle. In 20%-50% of familial cases of melanoma mutations are found in CDKN2A. The polymorphisms in the MC1R receptor, key in the formation of melanin in response to UV radiation, are also associated with an increased risk of melanoma
12	Melanoma maligno cutáneo en pacientes de la provincia de Las Tunas ^[13]	Descriptive study of transverse cut	Cutaneous melanoma predominated in the male sex, in the lower extremities and a late diagnosis was manifested in the patients, with the prevalence of Clark invasion level IV and the nodular melanoma as the most frequent histological type (AU)
13	Halo Nevó y Vitíligo: A propósito de un caso	Clinic Case	Malignant Melanoma is the most important differential diagnosis. For this, the characteristic of the halo is oriented: Symmetric and regular in the nevus, irregular and asymmetric in the melanoma. The characteristics of the pigmented lesion also matter, which must be evaluated according to the ABCD rule

(Contd...)

Table 1: (Continued)

14	Córdoba B, Alberto C. Melanoma nodular en borde de pie. Rev Cienc Méd 2014;18:329-36. Available from: http://www.scielo.sld.cu/scielo.php?script=sci_arttext&pid=S1561-31942014000200016&lng=es . [Last accessed on 2017 Oct 13]	Presentation of a case	Elderly patient with an asymptomatic lesion on the right foot, 4 years old, with rapid growth in the past 3 months. A clinical-histopathological diagnosis was made, compatible with nodular melanoma. The treatment of choice is surgical removal	Nodular melanoma is a very aggressive tumor and survival depends on an early diagnosis, enabling the healing >90% of cases
15	Santos VM, Leal CT, Vasconcellos MJ. Late diagnosis of nodular melanoma of the foot in a 74-year-old Brazilian man. Rev Med Chil 2011;139:1481-3.	Presentation of a case	We describe the late diagnosis of nodular melanoma of the foot in a 74-year-old Afro-Brazilian male	Surgery is the most effective treatment for MM in the early stages, and lymphadenectomy may be necessary. Treatment of late-stage melanoma includes chemotherapy, cryotherapy, drug combinations, radiation therapy, tumor injections, tumor-inhibiting chemical agents, and vaccines. The role of early diagnosis should be emphasized because MM is susceptible to cure if it is treated at an early stage. Skin lesions that suggest MM should be evaluated by a dermatologist before the biopsy since timely diagnosis and proper treatment prevent tumor spread
16	Cepeda-Valdés R, Skinner-Taylor C, Flores-Gutiérrez J, Alanís S. Metástasis en tránsito de melanoma maligno cutáneo: Reporte de caso y revisión de la bibliografía. Dermatología CMQ 2010;8:62-3. Available from: http://www.medigraphic.com/pdfs/cosmetica/dcm-2010/dcm101.pdf . [Last accessed on 2017 Nov 08].	Presentation of a case	A 64-year-old Hispanic female who presented metastasis after the surgical removal of malignant melanoma	The evolution of a patient undergoing the removal of malignant melanoma should be carefully reviewed by their treating physicians to diagnose early the probability of distant metastasis
17	Mar V, Roberts H, Wolfe R, English DR, Kelly JW. Nodular melanoma: A distinct clinical entity and the largest contributor to melanoma deaths in Victoria, Australia. J Am Acad Dermatol 2013;68:568-75.	Analysis of 4 Cohorts: 1989, 1994, 1999, and 2004. Four cohorts were established to perform the analysis, the original pathological reports were reviewed, and the melanoma	The incidence of thick tumors (4 mm) increased by 3.8% (95% confidence interval: 1.4–6.2) and 2.5% (95% confidence interval of 0.5–5.5) per year for male and female patients, respectively. The median thickness of the nodular melanoma at diagnosis was 2.6 mm compared to 0.6 mm for	The incidence of thick melanomas continues to increase. Nodular melanoma is clinically better differentiated and the predominant contributor to deaths related to melanomas. This represents a

(Contd...)

Table 1: (Continued)

<p>incidence rates standardized by age from 1989 to 2004 were compared with annual percentage change using the Poisson regression</p>	<p>superficial extension melanoma. One-third of patients who died of melanoma during the follow-up period had thick tumors (4 mm), most of which were nodular subtype (61%). Nodular melanoma accounted for 14% of invasive melanomas but was responsible for 43% of deaths from melanoma in a total of 57,461 years/person of follow-up. In comparison and superficial diffusion, melanoma contributed with 56% of invasive melanomas but only with 30% of deaths</p>	<p>A positive expression of BRAF-V600E, present in 86 (35%) of the cases, was found in a series of 248 positive patients with nodular melanoma, and it was significantly associated with an increase of the tumoral thickness, the presence of tumor ulceration and reduced survival. In addition, the expression BRAF-V600E was an independent prognostic factor, whereas the BRAF mutation status was not significant. There was 88% agreement between BRAF and V600E in the expression and status of the mutation</p>	<p>Review article</p>	<p>Early diagnosis and timely treatment are the only strategies to improve the prognosis of patients with melanoma</p>	<p>The incursion of immunotherapy is one of the main current therapies for this disease</p>
<p>18 Hugdahl E, Kalvenes MB, Puntvoll HE, Ladstein RG, Akslen LA. BRAF-V600E expression in primary nodular melanoma is associated with aggressive tumour features and reduced survival. Br J Cancer 2016;114:801-8.</p>	<p>Descriptive, observational article. In a series of 248 nodular melanoma positive patients, the total expression of BRAF and the presence of BRAF-V600E and total BRAF expression were evaluated using immunohistochemistry using tissue sections obtained by biopsy. The status of the mutation was evaluated using real-time PCR in cases with sufficient tumor tissue (n=191)</p>	<p>Review article</p>	<p>Review article</p>	<p>Review article</p>	<p>Review article</p>
<p>19 Gutiérrez-Vidrio RM, Cortés-Lozano M. Confrontando al melanoma en el siglo XXI. Med Cutan Iber Lat Am 2007;35:3-13. Available from: http://www.medigraphic.com/pdfs/cutaneal/mc-2007/mc071b.pdf. [Last accessed on 2017 Oct 27].</p>	<p>Review article</p>	<p>Review article</p>	<p>Review article</p>	<p>Review article</p>	<p>Review article</p>
<p>20 Camacho CP, Gerson R, Góngora MA, Villalobos A, Blanco YC, López O. Actualidades para el tratamiento del melanoma metastásico, estado del arte. Med Assoc Med Hosp ABC 2017;62:196-207. Available from: http://www.medigraphic.com/pdfs/abc/bc-2017/bc173g.pdf. [Last accessed on 2017 Oct 20].</p>	<p>(Cont...)</p>				

Table 1: (Continued)

21	Serna-Macías J, Sánchez-Casas N, Morato-López A, Reyes-García M, Isusi-Alcazar J. Melanoma maligno cutáneo. El rol del PET-CT. The role of PET-CT. GAMO. 2012;11(2):104-12. [citado 27 Oct 2017] Disponible: http://www.elsevier.es/es-revista-gaceta-mexicana-oncologia-305-articulo-melanoma-maligno-cutaneo-el-rol-X1665920112306599 .	Review article	Review article	The study of PET-CT with FDG and with diagnostic CT is the most accurate technique for the evaluation of MMC in Stages IIB and IIC, with positive sentinel lymph node test, and Stages III and IV
22	Gallegos J, Nieweg O. Melanoma cutáneo (MC): Diagnóstico y tratamiento actuales. Gac Méd Méx 2014;150 Suppl 2:175-82. Available from: http://www.medicgraphic.com/pdfs/gaceta/gm-2014/gms142g.pdf . [Last accessed on 2017 Oct [28].	Review article	Review article	Cutaneous melanoma is the third most frequent neoplasm in the skin and the one with the highest evolution toward mortality. The diagnostic approach is of great importance to achieve adequate therapy
23	Gaviria JL, Niño CJ. Melanoma: actualización en su enfoque y tratamiento. Universitas Médicas 2005;46:82-93. [citado 27 Oct 2017] Disponible en: https://www.redalyc.org/articulo.oa?id=231018663003&idp=1&cid=4342067	Review article	Review article	Its diagnosis is made through a thorough examination, identifying the suspicious changes of pre-existing injuries or new lesions. Its most relevant prognostic factor in determining the depth, as well as the presence or absence of positive nodes, presence or absence of ulceration and the presence or absence of distant metastases
24	Možuraitienė J, Bielskiene K, Atkociūs V, Labeikytė D. Molecular alterations in signal pathways of melanoma and new personalized treatment strategies: Targeting of Notch. Sci Direct 2015;51:133-45. Available from: https://www.acels-cdn.com/S1010660X15000439/1-s2.0-S1010660X15000439-main.pdf?_tid=8b930b8-c029-11e7-bd45-0000aab0f01&acdnat=1509667212_38129f5b44e3676927bc230c588309d1 . [Last accessed on 2017 Oct 24].	Review article	Review article	In this review, we summarize the data recently obtained about the new drug approved by the United States Food and Drug Administration for the treatment of metastatic melanoma and the treatment strategy model when targeting the Notch gene

(Contd...)

Table 1: (Continued)

<p>25 Yeh I. Recent advances in molecular genetics of melanoma progression: Implications for diagnosis and treatment. <i>Frac Rev</i> 2016;11:529:1-8. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4926755/pdf/f1000research-5-8869.pdf. [Last accessed on 2017 Oct 29].</p>	<p>Review article</p> <p>It is necessary to resort to genetic findings to complement the diagnosis and resort to more specific treatments. Genetic progression models will help us develop better clinical and biological hypotheses to direct future research in the area of melanomas</p>
<p>26 Rigel D, Russak J, Friedman R. The evolution of melanoma diagnosis: 25 years beyond the ABCDs. <i>Cancer J Clin</i> 2010;60:1-16. Available from: http://www.onlinelibrary.wiley.com/doi/10.3322/caac.20074/epdf. [Last accessed on 2017 Oct 27].</p>	<p>Review article</p> <p>A "good clinical eye" remains essential to select suspicious lesions and evaluate them early. As current approaches are refined and new techniques are developed, the improved ability to diagnose this cancer will improve while achieving the goal of reducing melanoma mortality</p>

PCR: Polymerase chain reaction, PET-CT: Positron emission tomography-computed tomography, FDG: Fludeoxyglucose, UV: Ultraviolet

The first 5 years of follow-up after removing melanoma are the most important since 90% of all metastases occur during this period.^[11] Follow-up should be done at 3-month intervals in the first 3 years and subsequently every year.^[12] The skin should be examined at depth, including the scalp and genital region, particularly in the regional distribution of primary palpation, and the lymph nodes, with attention to the regional lymph node chain, in addition to offering psychosocial support and W of the private sector in the states of Guadalajara and Monterrey. In the country, there are only two public-level teams of this type that are located in the Autonomous University of Mexico and the ABC Medical Center, so their access is complicated for their authorization together with their high cost.

The standard of treatment for melanoma metastasis is surgical intervention, and its goal is to provide relief of symptoms and increase survival time. Due to the great possibility of metastasis at the level of the central nervous system, prophylactic radiotherapy can be considered, as was done in the patient.^[23]

In a meta-analysis of 3262 patients with malignant melanoma, it was found that single drug chemotherapy is well tolerated, but is associated with response rates of only 5–20%.^[24] In addition, combination chemotherapy and biochemotherapy may raise response rates, but they do not prolong survival and cause greater toxicity.^[25]

Immunotherapeutic approaches, such as high doses of interleukin 2, are associated with durable responses in a small percentage of patients.^[26] In the case of the patient, chemotherapy was adjuvant with excisional surgery due to the advanced stage of the disease. The chemotherapeutic treatment used in the patient complies with the internationally recommended scheme consisting of pegylated interferon with ipilimumab.^[26]

At present, some of the main pathways of melanoma progression are better understood, and it is likely that molecular techniques (specific genomic incorporation and intratumoral expression) play an essential role in making classification schemes that have more power in predicting response to therapy.^[27]

It is vital to inform the general population of the risk of suffering from melanoma, especially from the premise of multiple nevi and prolonged exposure to the sun, so that, in an almost routine and obligatory way, it would be the use of appropriate clothing such as hats wide-brimmed, clothing that covers most of the body, the use of sunscreen filters (especially in childhood and adolescence) and self-assessment with application of the ABCDE method.

Melanomas and skin cancers are generally painless, but in this patient, the degree of depth of invasion, as well as the perineural compromise and ulceration, made it painful.

Health personnel and patients should be alert to injuries. In case of suspicion of metastatic melanoma, the diagnostic criteria should be applied and the diagnosis confirmed with biopsy and histopathological study, since early identification is decisive. Follow-up must be done to establish the diagnosis in a timely manner.

REFERENCES

- Fuente-García AD, Ocampo-Candiani J. Melanoma cutáneo. Gac Med Mex 2010;2:146. Available from <http://www.medigraphic.com/pdfs/gaceta/gm-2010/gm102i.pdf>. [Last accessed on 2017 Sep 24].
- Frías AG, Ortiz HC, Lara HM. Estudio epidemiológico de melanoma maligno en el American British Cowdry medical center. Ann Med 2011;56:196-204. Available from <http://www.medigraphic.com/pdfs/abc/bc-2011/bc114d.pdf>.
- Hernández-Zárate S, Medina-Bojórquez A, López-Tello Santillán A, Alcalá-Pérez D. Epidemiología del cáncer de piel en pacientes de la clínica de dermatooncología del centro dermatológico Dr. Ladislao de la Pascua. Estudio retrospectivo de los últimos ocho años. Dermatología Rev Mex 2012;56:30-7. Available from <http://www.medigraphic.com/pdfs/derrevmex/rmd-2012/rmd121e.pdf>. [Last accessed on 2017 Sep 24].
- Arenas R. Atlas Dermatología, Diagnóstico y Tratamiento. 3rd ed. México: McGraw-Hill Interamericana; 2009.
- Jurado-Santa CF, Medina-Bojórquez A, Gutiérrez-Vidrio RM, Ruiz-Rosillo JM. Prevalencia del cáncer de piel en tres ciudades de México. Rev Med Inst Mex Seguro Soc 2011;49:253-8. Available from <http://www.medigraphic.com/pdfs/imss/im-2011/im113f.pdf>. [Last accessed on 2017 Oct 15].
- Güémez-Graniel MF, Plascencia-Gómez A, GranieL-Lavadores MJ, Dzul-Rosado K. Epidemiología del cáncer de piel en el Centro Dermatológico de Yucatán durante 2012. Dermatol Rev Mex 2015;59:9-18. Available from <http://www.medigraphic.com/pdfs/derrevmex/rmd-2015/rmd151c.pdf>. [Last accessed on 2017 Oct 22].
- Calderón L, Peniche-Castellanos A, Fierro-Arias L, Montes de Oca-Sánchez G, Arellano-Mendoza I. Melanoma cutáneo: 12 años de experiencia. Dermatol Rev Mex 2017;61:179-89. Available from: <http://www.medigraphic.com/pdfs/derrevmex/rmd-2017/rmd173b.pdf>.
- Hunter A, Boris C. From melanocytes to melanomas. Nature 2016;16:345-58. Available from <https://www.nature.com/nrc/journal/v16/n6/pdf/nrc.2016.37.pdf>. [Last accessed on 2017 Oct 24].
- Gallegos Hernández JF, Melanoma C. Fundamentos del diagnóstico y la terapéutica. Acta Med Gpo 2012;10:207-13. Available from <http://www.medigraphic.com/pdfs/actmed/am-2012/am124h.pdf>.
- Acosta DA, Bravo A, Ruíz D, Acosta GM. Comportamiento del cáncer de piel en Güines y San José de las Lajas. Rev Habana Cienc Méd 2014;20:44-53. Available from <http://www.medigraphic.com/pdfs/reviemedhab/cmh-2014/cmh141f.pdf>. [Last accessed on 2017 Oct 20].
- Mangas C, Paradelo C, Puig S, Gallardo F, Marcoval J, Azon A, et al. Valoración inicial, diagnóstico, estadificación, tratamiento y seguimiento de los pacientes con melanoma maligno primario de piel. Documento de consenso de la “xarxa de centres de melanoma de Catalunya i Balears”. Actas Dermatosifiliogr. 2010;101:129-42. Available from <http://www.actasdermo.org/es/valoracion-inicial-diagnostico-estadificacion-tratamiento/articulo/S0001731010000591>. [Last accessed on 2017 Oct 24].
- Acosta AE, Fierro E, Velásquez VE, Rueda X. Melanoma: Patogénesis, clínica e histopatología. Rev Assoc Col Dermatol 2009;17:87-108. Available from: <http://wwwantoniorondonlugo.com/blog/wp-content/uploads/2009/08/revision-m-elanomas.pdf>.
- Palomo AM, Pérez MD, Pérez OR, Yabor VD, Fontaine AM. Melanoma maligno cutáneo en pacientes de la provincia de Las Tunas. Revista electrónica Dr. Zoilo E. Marinello Vidaurreta 2015;12:40. Available from: <http://www.revzoilomarinello.sld.cu/index.php/zmv/article/view/483>.
- Aldama C, Arnaldo B, Victoria R, Graciela G, Liz D, Olga A, et al. Halo Nevo y Vitílico: A propósito de un caso. Pediatrics 2007;34:31-3. Available from http://www.scielo.iics.una.py/scielo.php?script=sci_arttext&pid=S1683-98032007000100005&lng=en. [Last accessed on 2017 Oct 04].
- Córdoba B, Alberto C. Melanoma nodular en borde de pie. Rev Cienc Méd 2014;18:329-36. Available from http://www.scielo.sld.cu/scielo.php?script=sci_arttext&pid=S1561-31942014000200016&lng=es. [Last accessed on 2017 Oct 13].
- Santos VM, Leal CT, Vasconcellos MJ. Late diagnosis of nodular melanoma of the foot in a 74-year-old Brazilian man. Rev Med Chil 2011;139:1481-3.
- Cepeda-Valdés R, Skinner-Taylor C, Flores-Gutiérrez J, Alanís S. Metástasis en tránsito de melanoma maligno cutáneo: Reporte de caso y revisión de la bibliografía. Dermatología CMQ 2010;8:62-3. Available from <http://www.medigraphic.com/pdfs/cosmetica/dcm-2010/dcm1011.pdf>. [Last accessed on 2017 Nov 08].
- Mar V, Roberts H, Wolfe R, English DR, Kelly JW. Nodular melanoma: A distinct clinical entity and the largest contributor to melanoma deaths in Victoria, Australia. J Am Acad Dermatol 2013;68:568-75.
- Huggdahl E, Kalvenes MB, Puntervoll HE, Ladstein RG, Akslen LA. BRAF-V600E expression in primary nodular melanoma is associated with aggressive tumour features and reduced survival. Br J Cancer 2016;114:801-8.
- Gutiérrez-Vidrio RM, Cortés-Lozano M. Confrontando al melanoma en el siglo XXI. Med Cutan Iber Lat Am 2007;35:3-13. Available from <http://www.medigraphic.com/pdfs/cutanea/mc-2007/mc071b.pdf>. [Last accessed on 2017 Oct 27].
- Camacho CP, Gerson R, Góngora MA, Villalobos A, Blanco YC, López O. Actualidades para el tratamiento del melanoma metastásico, estado del arte. Med Assoc Med Hosp ABC 2017;62:196-207. Available from <http://www.medigraphic.com/pdfs/abc/bc-2017/bc173g.pdf>. [Last accessed on 2017 Oct 20].
- Serna-Macías J, Sánchez-Casas N, Morató-López A, Reyes-García M, Isusi-Alcazar J. Melanoma maligno cutáneo. El rol del PET-CT. GAMO. 2012;11(2):104-12. Disponible en: <http://www.elsevier.es/es-revista-gaceta-mexicana-oncologia-305-articulo-melanoma-maligno-cutaneo-el-rol-X1665920112306599>
- Gallegos J, Nieweg O. Melanoma cutáneo (MC): Diagnóstico y tratamiento actuales. Gac Méd Méx 2014;150 Suppl 2:175-82. Available from <http://www.medigraphic.com/pdfs/gaceta/>

- gm-2014/gms142g.pdf. [Last accessed on 2017 Oct 28].
24. Gaviria JL, Niño CJ. Melanoma: actualización en su enfoque y tratamiento. Universitas Médicas 2005;46:82-93. Disponible en: <https://www.redalyc.org/articulo.oa?id=231018663003&idp=1&cid=4342067>.
25. Mozūraitienė J, Bielskienė K, Atkočius V, Labeikytė D. Molecular alterations in signal pathways of melanoma and new personalized treatment strategies: Targeting of Notch. Sci Direct 2015;51:133-45. Available fromhttps://www.ac.els-cdn.com/S1010660X15000439/1-s2.0-S1010660X15000439-main.pdf?_tid=8b9300b8-c029-11e7-bd45-00000aab0f01&a_cdnat=1509667212_38129f5b44e3676927bc230c588309d1. [Last accessed on 2017 Oct 24].
26. Yeh I. Recent advances in molecular genetics of melanoma progression: Implications for diagnosis and treatment. Fac Rev 2016;1529:1-8. Available from<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4926755/pdf/f1000research-5-8869.pdf>. [Last accessed on 2017 Oct 29].
27. Rigel D, Russak J, Friedman R. The evolution of melanoma diagnosis: 25 years beyond the ABCDs. Ca Cancer J Clin 2010;60:1-16. Available from<http://www.onlinelibrary.wiley.com/doi/10.3322/caac.20074/epdf>. [Last accessed on 2017 Oct 27].

How to cite this article: Valeria JM, Margarita CC, Elizabeth RA, Ludivina M, Jurado LS, Hernandez MMC, Bogarín ELU. Nodular Malignant Melanoma. Asclepius Med Case Rep 2019;2(1):1-13.