Cutaneous and mucosal melanoma

Czerniak skóry i błon śluzowych

*Piotr Sobolewski[1], Klaudia Dopytalska[1], Marek Roszkiewicz[1], Agata Mikucka-Wituszyńska[1], Elżbieta Szymańska[1], Irena Walecka[1,2]**

[1] *Dermatology Department, Centre of Postgraduate Medical Education, Warsaw, Poland*
[2] *Dermatology Department, Central Hospital of Ministry of Internal Affairs, Warsaw, Poland*

KEYWORDS:

- cutaneous melanoma
- mucosal melanoma
- diagnosis, treatment

ABSTRACT

Malignant melanoma (MM) still remains a potentially fatal disease despite the fact that advanced diagnostic methods and modern therapeutic options are available. Melanoma is a cancer deriving from neuroectodermal melanocytic cells. The standardized incidence rate of melanoma in Poland is 4,9 per 100 000. The mucosal melanoma is a rare form of this cancer accounting for only 2% of the diagnosed cases. The fast diagnosis and surgical treatment are the keys to decreased mortality. In metastatic disease systemic therapy is needed but no highly efficient drug has been identified yet. This paper concentrates on introduction of elemental knowledge about melanoma to raise awareness among medical professionals of different specialities in order not to overlook any case of melanoma.

SŁOWA KLUCZOWE:

- czerniak skóry
- czerniak błony śluzowej
- rozpoznanie
- leczenie

STRESZCZENIE

Czerniak wciąż pozostaje potencjalnie śmiertelną chorobą, pomimo dostępności zaawansowanych metod diagnostycznych i nowoczesnych opcji terapeutycznych. Czerniak jest nowotworem wywodzącym się z neuroektodermalnych komórek melanocytowych. Standaryzowany współczynnik zachorowalności w Polsce wynosci 4,9 na 100 000. Czerniak błon śluzowych jest rzadką formą tego nowotworu dotyczącą 2% rozpoznań. Szybka diagnostyka i leczenie chirurgiczne jest kluczem do zmniejszenia śmiertelności. W przypadku obecności przerzutów odległych terapia systemowa jest konieczna. Jednak lek o wysokiej skuteczności nie jest jeszcze dostępny. W opracowaniu przedstawiono najważniejsze aspekty czerniaka, aby zwiększyć świadomość wśród lekarzy różnych specjalności. Pozwoli to uniknąć przeoczenia rozpoznania czerniaka.

Epidemiology

In Poland melanoma occurs rarely – the standardized incidence rate is 4,9 per 100 000 which means about 3100 new cases in a year (1). In the USA general rate in the white population was 27,5 per 100,000 and in the black population it was 1,1 per 100,000 (2). The highest rates were reported in New Zealand (35,8 per 100 000) and Australia (34,9 per 100 000) (3). In contrary to other malignant tumors melanoma occurs mostly in young and middle-aged people, the mean age at the time of diagnosis of melanoma is 57. Generally, men are more susceptible than women to this type of cancer, but it should be reviewed in relationship to age group: the incidence rate in patients younger than 40 is greater in women, and after by the age of 75 years the incidence rate in men triples (4-5).

The mucosal melanoma is a rare form of this cancer accounting for only 2% of all diagnosed cases (6). It can occur within any mucosal surface, but the vast majority develop in the mucosae of the head and neck (31% to 55%), anorectal (17% to 24%) and vulvovaginal (18% to 40%) regions (7-8). Less frequently melanomas arise in the mucosae of the urinary tract, pharynx, larynx, esophagus, and cervix. Very rarely there are cases described in the literature of melanoma metastases in the lymph nodes confirmed by the histopathological examination without any primary skin melanoma present. It obliges clinicians to perform all the available screening methods (gastrofiberoscopy, colonoscopy, colposcopy, tracheoscopy) to find the primary site of cancer. The mean age of diagnosis differs from skin melanoma, and occurs mostly in patients in the 7th decade of life. As the mucosal melanoma is also diagnosed in the more advanced stage, the 5-year overall survival rate is worse – 25% for mucosal melanoma compared to 80% for cutaneous melanoma (Fig. 1,2) (8).

Risk factors

Melanoma is nowadays considered to be a multifactorial cancer. The influence of UV radiation on incidence risk

*Address: *Irena Walecka, Dermatology Department, Centre of Postgraduate Medical Education, ul. Wołoska 137, 02-507 Warszawa.*
e-mail: irena.walecka@cskmswia.pl
ISSN 2657-9669/
Published by Centrum Medyczne Kształcenia Podyplomowego

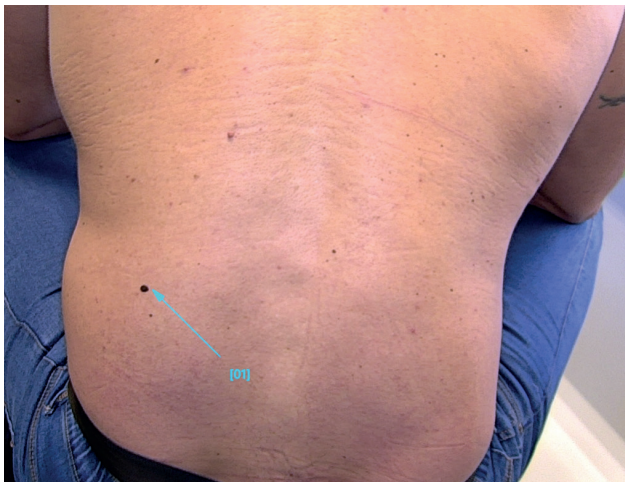

Fig. 1. 41 year old patient with melanoma in left lumbar area – macroscopic view.

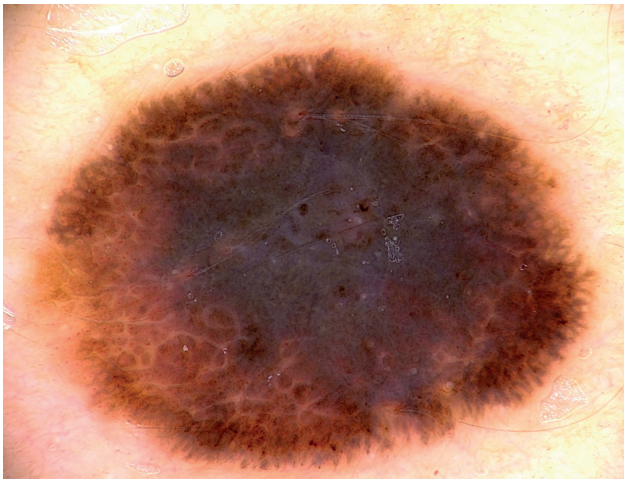

Fig. 2. Melanoma in stage pT1b in-patient from fig. 1 – videodermoscopic picture.

is scientifically proven. It should be emphasized that intermittent sun exposure and a history of sunburns in childhood are the risk factors of melanoma, whereas the chronic continuous pattern of exposure is more connected with non-melanoma skin cancer (NMSC) (9).

Genetic susceptibility is considered to be a risk factor of MM. The family history of melanoma increases the possibility of this cancer in patients. Additionally, some genetic disorders associated with higher melanoma risk have been described: familial atypical mole syndrome, familial retinoblastoma, Li-Fraumeni cancer syndrome and Lynch syndrome type II (10).

The lower photo-types of the skin raise the risk of developing MM, and the features: red hair, light skin, multiple freckles, light eyes, sun oversensitivity can increase the rate by approximately 50% (11).

The important melanoma risk factor is the number of nevi as 25% of MM develops in a preexisting nevus. The more nevi patient has, the higher the risk of developing melanoma during a lifetime – more than 100 nevi raise the rate 7 times (12). Also, the size of the nevus is crucial: in larger (>5 mm) and giant (>20 cm) nevi, the possibility of melanoma is significantly higher (13).

Diagnosis and management

The basic method used in the diagnosis of melanoma is the careful examination of the skin using dermoscopy or video dermoscopy. The clinical and diagnostic examination should also include those hard to reach parts of the body: scalp, palms and soles, interdigital spaces and sex organs. The dermoscopy of nevi increases the diagnostic sensitivity of up to 30%. The several algorithms for analyzing the dermoscopic views are available. The rudimentary one – 3-point scale – enables the physician to make the diagnosis of MM with 96,3% of sensitivity and 94,2% of specificity (1). The routine dermoscopy of melanocytic lesions should be performed every 3 years in patients under the age of 40 and every year thereafter. In dysplastic nevus syndrome examination is recommended every 6 months, and video dermoscopy appears to be the best method (Fig. 3,4).

In doubtful cases (facial nevi, large congenital nevi, mucosal nevi, dysplastic nevus syndrome) the reflectance confocal microscopy (RCM) is recommended. In 2005 Pellacani et al. created RCM guidelines for the diagnosis of melanoma and such examination can increase the accuracy to nearly 100%. This method can be used to select an in vivo biopsy site and assess surgical margin (14).

The final diagnosis is made after the surgical excision of the suspected nevus with the margin of 1-2 mm of unaltered skin. The punch biopsy is allowed only in lentigo simplex of the face when the lesion is large. The preventive nevi excision is not recommended.

The histopathological report of melanoma should be composed of a standardized macro – and microscopic evolution of cancer according to the 7th edition of pathomorphological TNM AJCC/UICC classification (15).

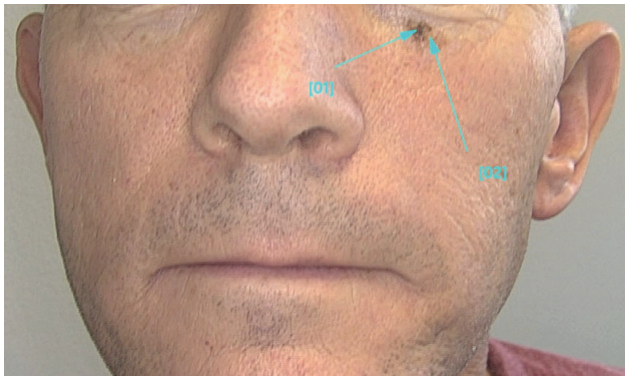

Fig. 3. 54 year old patient with melanoma in left infraorbital site – macroscopic view.

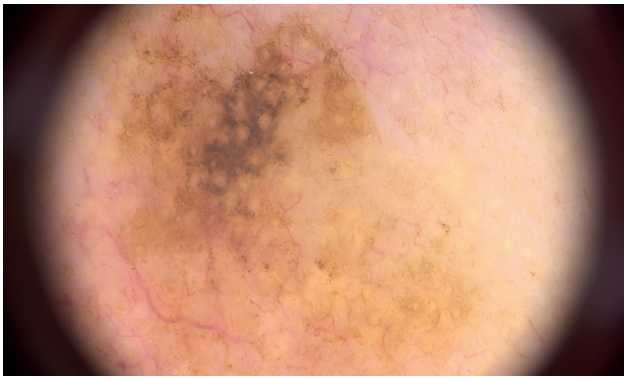

Fig. 4. Melanoma in situ in patient from fig. 3.

The therapeutic decisions are made based on the microscopic and clinical staging of melanoma. The melanoma team of experts should be composed of a dermatologist, oncologist, surgeon and in individual cases also otolaryngologist, urologist, and gynecologist. In cutaneous low-advanced melanoma, the primary excision with the sequential widening of surgical margins remains the only possible intervention. More infiltrative cases of melanoma require an additional biopsy of the sentinel lymph node. The metastatic disease is determined after radiologic examinations of the patient. The therapeutic lymphadenectomy and adjuvant therapy (chemotherapy, radiotherapy) are then obligatory. Unfortunately, wide negative margins are difficult to achieve in mucosal melanoma due to anatomic constraints, disease multifocality or a lentiginous growth pattern. It contributes to the high rate of recurrences in most mucosal melanomas, which obliges clinicians to introduce adjuvant radiotherapy in less locally advanced cases (16). Chemotherapy of melanoma is comprised of classical cytotoxic agents (dacarbazine, cisplatin, vinblastine, carmustine) and immunotherapeutics (anty-CTLA4 and anty-PD-1 monoclonal antibodies). The results of this treatment are still unsatisfactory – the average survival period is 6-12 months and only 10% of patients reach the 5-year-survival criterion. Molecularly targeted treatment of melanoma (BRAF and MEK inhibitors) is nowadays available and the median survival period in individual cases can be extended to 20-25 months. Nevertheless, further studies are needed (1).

The follow-up period of 5 years in melanoma patients includes frequent dermoscopic examination, regular investigation of lymph nodes by palpation and ultrasound and screening of metastatic disease with the use of screening technics (radiograph of the chest, ultrasound of the abdomen, serum level of liver enzymes and lactate dehydrogenase – LDH). When the patient presents with the symptoms of metastases (elevated liver enzymes and/or LDH, bone pain, chronic cough or neurological signs) the more advanced diagnostic imaging must be performed (CT, MRI, scintigraphy).

Conclusions

Despite the very efficient diagnostic methods that are available at the moment and the possibility of fast diagnosis and treatment, which can assure the full recovery of the patient, the mortality rates still remain high. The occurrence of the mucosal melanoma is not statistically high, but when occurs – it dramatically worsens the prognosis. The locally advanced and metastatic melanoma is still considered as the fatal disease for the lack of efficacious treatment. The awareness of potential risk factors amongpatients and physicians of different specialities is crucial to increase the diagnosis of melanoma in the initial stages. Regular dermoscopy of nevi is a cheap, simple, available examination and should be performed in every patient. The organization of disease-oriented campaigns (Melanoma Day, Euromelanoma) brings great results in increasing the public awareness and is an important part of preventive medicine.

References

(1) Rutkowski P, Wysocki PJ, Nasierowska-Guttmejer A, Fijuth J, Kalinka-Warzocha E, Świtaj T et al. Cutaneous melanoma – guidelines for diagnostics and therapy in 2016. Dermatology Review 2016; 103(1):1-18. DOI:10.5114/dr.2016.57736.

(2) Rastrelli M, Tropea S, Rossi CR, Alaibac M. Melanoma: epidemiology, risk factors, pathogenesis, diagnosis and classification. In Vivo 2014 Nov-Dec; 28(6):1005-11.

(3) Matthews NH, Li WQ, Qureshi AA, Weinstock MA, Cho E. Epidemiology of Melanoma. In: Ward WH, Farma JM (eds). Cutaneous Melanoma: Etiology and Therapy. Codon Publications. Brisbane (AU); 2017 Dec 21.

(4) Rigel DS. Epidemiology of melanoma. Semin Cutan Med Surg 2010; 4: 204-209.

(5) Lasithiotakis K, Leiter U, KrügerMacKie RM, Hauschild A, Eggermont AM. Epidemiology of invasive cutaneous melanoma. Ann Oncol 2010; 20 (Suppl 6): vi1-7.

(6) Lerner BA, Stewart LA, Horowitz DP, Carvajal RD. Mucosal Melanoma: New Insights and Therapeutic Options for a Unique and Aggressive Disease. Oncology (Williston Park) 2017 Nov 15; 31(11):e23-e32.

(7) Chang AE, Karnell LH, Menck HR. The National Cancer Data Base report on cutaneous and noncutaneous melanoma: a summary of 84,836 cases from the past decade. The American College of Surgeons Commission on Cancer and the American Cancer Society. Cancer 1998; 83:1664-78.

(8) McLaughlin CC, Wu XC, Jemal A, et al. Incidence of noncutaneous melanomas in the U.S. Cancer 2005; 103:1000-7.

(9) Elwood JM, Jopson J. Melanoma and sun exposure: an overview of published studies. Int J Cancer 1997; 73: 198-203.

(10) Markovic SN, Erickson LA, Rao RD, Weenig RH, Pockaj BA, Bardia A, Vachon CM, Schild SE, McWilliams RR, Hand JL, Laman SD, Kottschade LA, Maples WJ, Pittelkow MR, Pulido JS, Cameron JD, Creagan ET and Melanoma Study Group of the Mayo Clinic Cancer Center. Malignant melanoma in the 21st century, part 1: epidemiology, risk factors, screening, prevention, and diagnosis. Mayo Clin Proc 2007; 3: 364-380.

(11) Titus-Ernstoff L, Perry AE, Spencer SK, Gibson JJ, Cole BF and Ernstoff MS. Pigmentary characteristics and moles in relation to melanoma risk. Int J Cancer 2005; 116: 144-149.

(12) Gandini S, Sera F, Cattaruzza MS, Pasquini P, Abeni D, Boyle P and Melchi CF. Meta-analysis of risk factors for cutaneous melanoma: I. Common and atypical naevi. Eur J Cancer 2005; 41: 28-44.

(13) Watt AJ, Kotsis SV and Chung KC. Risk of melanoma arising in large congenital melanocytic nevi: a systematic review. Plast Reconstr Surg 2004; 113: 1968-1974.

(14) Pellacani G, Cesinaro AM, Seidenari S. Reflectance-mode confocal microscopy of pigmented skin lesions – improvement in melanoma diagnostic specificity. J Am Acad Dermatol 2005; 53, 979-985.

(15) Edge SE, Byrd DR, Carducci MA, Compton CA, eds. AJCC Cancer Staging Manual. 7th ed., NY: Springer. New York 2009.

(16) Carvajal RD, Spencer SA, Lydiatt W. Mucosal melanoma: a clinically and biologically unique disease entity. J Natl Compr Canc Netw 2012; 10:345-56.