GENERAL CONSIDERATIONS REGARDING THERPEUTIC AND CLINICAL ASPECTS ON CUTANEOUS MELANOMA

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Abstract

Melanoma is a malignant tumor of melanocytes, whose incidence has increased dramatically in recent years and is a substantial public health problem. The incidence is high among young people, one of the 5 patients develop metastases leading to death. Environmental factors that lead to intense or intermittent exposure (weekends, holidays) UV (UVA and UVB), multiple sunburns, early childhood exposure, increase the incidence of cutaneous melanoma, in recent years it was in continuous ascent, with the largest rate of growth of malignant tumors. Timely detection of problematic injuries and prompt surgical excision increased survival rate. Early screening with improved diagnostic techniques, new immunological and molecular research targeting more advanced stage of melanoma cutaneous melanoma may influence the future.

Key words: melanoma, UV radiation, incidence, melanoma prognostic, melanoma treatement.

INTRODUCTION

Melanoma etiology is still unknown. There are several risk factors including among the most important: genetic factors, skin phototype, gender, pre-existing melanoma lesions, environmental factors, immunosuppression. The role of genetic factors is not known exactly,1-11% are familial cases, autosomal dominant transmission is done, four genes are mainly involved: chromosomes 1p, 6q, 7 and9, 9p21 tumor suppressor gene, deletions and rearrangement of chromosomes 10 and 11 (Muresan Mihai 2007). Most exposed people are phototype I and II, the people with pale skin (blond, redheads, blue eyes). The incidence of melanoma is 2 times higher in females, this hypothesis being supported by the existence of estrogens, knowing that cutaneous melanoma worsens during pregnancy (Forsea et al. 1998). Nevocellulary nerves present in large numbers, efelideles, multiple dysplastic nerves are other important risk factors.

Chronic and cumulative exposure to UV radiation (sunlight, tanning salons) of persons with phototype I and II increase the incidence of cutaneous melanoma. (Jose M.Pimiento et al 2013). Individuals who work outdoors are less exposed to cutaneous melanoma, than people working in the indoor environment and recreationaly exhibit themselves to short periods UV radiation. (Bologna L Jean et al 2009). Intense intermittent exposure (weekend leave) or artificial radiation (tanning salons) increase

the risk of skin cancer by 1.3 times. Early and prolonged exposure in childhood sa well as multiple sunburns also increase the risk of cutaneous melanoma.(Lens MB et al 2004). One or two episodes of sunburn increase the risk of skin cancer three fold, and three or more episodes of sunburn increase the risk of skin cancer seven fold. Transplant and immunosuppression increase the risk of skin cancer three fold.(Lens MB et al 2004).

MATERIAL AND METHOD

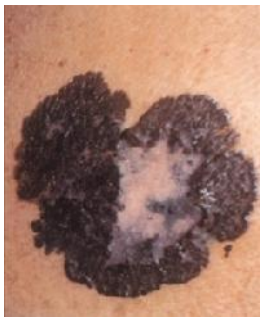
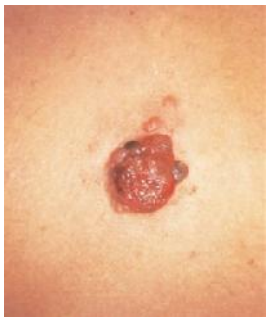
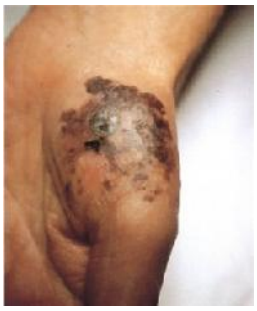
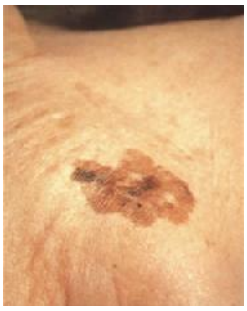
The rate of cutaneous melanoma incidence and mortality continued to increase during the recent years in all parts of the world, being a great public health problem. Melanoma represents 4% of all malignant tumors, the annual incidence increased by 5-12% and is doubling every 30 years, being the form of cancer with the highest growth rate of all cancers. The mortality rate has declined in recent years due to early diagnosis and numerous screenings performed. The highest incidence of melanoma in Australia is 50 pers/100,000 people (1:20). In Europe melanoma incidence rate began to rise from 1950 when many Europeans began to travel south for sunbathing. In the U.S. in 2005, 59,000 Americans were diagnosed with melanoma and 7700 died, the incidence increased from 1/100,000 inhabitants to 15 / 100,000 inhabitants (Bologna L Jean et al 2009). In 2001, in the UK, the incidence of melanoma is 12.4 / 100,000 inhabitants with a mortality rate of 3/100000 inhabitants (http://www.cancerresearchuk.org/) and 1:300 in Romania (Eniu Dan 2007).

There are 4 clinico-pathological forms: melanoma extensive area, lentigo malignant melanoma, nodular melanoma, acral melanoma (Table I). The most common of cutaneous melanomas with over 70% coverage, is the surface extensively melanoma, localized on legs in women and on the trunk in men. Nodular melanoma has the more reserved prognosis, and it appears frequently on the head, neck and torso. Acral melanoma occurs in 10% of cases being located palmar, plantar or on fingers. Melanoma occured in a preexisting lesion of lentigo malignant is located on fotoexposed areas in 5% of cases.(Bologna L Jean et al 2009).

All melanoma lesions have irregular aspect, rapid extension of resorption pigment, reddish-brown or blackish-blue colour, skin normally disappears, they have variable diameter from a few millimeters to 10 cm, very rapid evolution and prognosis in most of the cases is reserved (Forsea et al 1998).

Table 1

Clinical presentation of melanoma

Superficial Spreading	Nodular
	
Acral Lentiginous	Lentigo Maligna
	

RESULTS AND DISSCUSION

Among histological prognostic the most important factors to be taken into account are: Clark index which measures the depth extension of the tumor into 5 stages, and Breslow index that measures the maximum tumor thickness in mm, measured from the granular layer to its deepest part.(Forsea et al 1998). Correlation between Breslow index and Clark level of invasion and survival at 5 years is: Breslow < 0,76 mm survival rate 96-97 % at Breslow > 4mm survival rate 49 %; Clark level II have a 5 year survival rate 95% and Clark level V have a survival rate 49% at 5 year. Microscopic or macroscopic nodes involved in regional lymph metastasis are associated with 5 year survival rate of 38-78%, the number of nodes involved makes the difference. For distant metastatic disease the prognostic with median survival of only 6-9 month (Jonathan B. Heistein et al).

Another important criterion for prognostic and diagnosis would be the dermoscopy, which is a noninvasive method for early diagnosis of early stages of melanoma from benign lesions. The mnemonic formula for early melanoma (early stage melanoma ABCDE rule):

A- (lesion **a**symetry)
B- (irregular **b**order)
C- (**c**olor variegation)
D- (**d**imension)
E- (**e**nlargement, **e**volution)

Melanoma is a very aggressive tumor and has rapid metastasis, the prognosis depends on tumor thickness, level of inavasion, mitotic activity, clinical form, location. The higher number of visceral or lymph node metastases lowers the life expectancy. 5-year survival is higher in women, and younger people have a better prognosis(Forsea et al 1998).

Any skin lesion that shows changes in size, color, shape or is associated with ulceration, itching, bleeding or crusting should be biopsied. Biopsy diagnosis aims at a correct diagnosis of cutaneous melanoma on staging and appropriate treatment according to the case. Incisional biopsy is to approach difficult anatomic areas (face, subungual) or 1-2 mm excision healthy skin piece is to be sent for histopathological examination.(Jonathan B. Heistein). The choice of therapeutic strategy is based on the clinical and tumor stage. In stages I and II the treatment is completed by surgical excision of the tumor with safety margins that vary depending on the thickness of the lesion between 1-3 cm, without exceeding the fascia, there is no evidence that removing them would be useful (Richard Danialan et al 2012). As a prophylactic lymphadenectomy is an issue much discussed, not indicated in melanomas with thickness less than 0.75 mm and greater than 3 mm, sentinel lymph node biopsy is a choice. In stage III, practiced surgical excision with margins of safety 3cm, wide regional lymphadenectomy, inteferon alpha - 2b, adjuvant chemotherapy and biological therapy, being to being evaluated. In stage IV metastasis practice surgical excision, radiotherapy symptomatic trials of systemic chemotherapy, biological agents, alpha -2b IFN, IL -2 activated lymphocytes, chemoimunoterapie, biochemoterapie and therapies are being evaluated with biological agents, intralesional injections with BCG, new chemotherapeutic agents, regional hyperthermia perfusion with isolated limb mephalan (Eniu Dan 2007). Dispensary is 6 months in the first 2 years and then annually.

CONCLUSIONS

Cutaneous melanoma is a serious and unpredictable disease, although curable in the early stages, it is developing devastating disseminated stage, 12 women and 7 men die daily from cutaneous melanoma. Under 40 years, ¼ of cutaneous melanomas are appearing, and in women between 20 and 35 years take place as mortality, its incidence being in continuous growth (50% in the last 10 years).

Avoid sun exposure between the hours 10-16, sunscreen creams (SPF 30-50), umbrellas, hats, sunscreen clothing, avoid sunburn, sun exposure and gradually increased attention on individuals at risk as well as discouraging the attendance to tanning salons, are some of the methods of preventing the occurrence of skin cancer.

Population education programs, screening programs, excision of suspicious pigmentation nerves, early detection, continuation of clinical trials, careful physical examination, and searches for genetic and serum markers are some of the objectives that would lead to lower the occurence of this silent disease.

REFERENCES

1. Bologna L Jean, Joseph L Jorizzo, Ronald P Raini: Dermatology, Second Edition, 2008, pp. 1745-1769.
2. Bonnie E. Gould Rothberg, Michael B. Bracken, David L. Rimm. Tissue Biomarkers for prognosis in cutaneous melanoma: a systematic review and metaanalysis. J Natl Cancer Inst.2009;101(7):452-474.
3. Eniu Dan. Skin Melanoma, Clinical and Surgical Aspect. „Ion Chiricuta" Oncology Institute 2007
4. Forsea A.M., V.del Marmol, E.E. Bailey, A.C. Geller. Melanoma incidence and mortality in Europe. The British Journal of Dermatology. 2012;167(5):1124-1130.
5. Forsea Dan, Raluca Popescu, Catalin Mihai Popescu, Compendiu de dermatologie si venerologie. Editura tehnica 1998.
6. Heather G Gatcombe, MD. Advances Melanoma Management.2006 apr 17. Oncology Congress.
7. Idorn L. W., P.A. Philipsen, H.C. Wulf. Sun exposure before and after a diagnosis of cutaneous malignanat melanoma. The British Journal of Dermatology. 2011;165(1):164-170.
8. Jade Homsi, MD, Mohamed Kashani-Sabet, MD, Jane L. Messina, MD, Adil Daud, MD. Cutaneous Melanoma: Prognostic Factors. Cancer Control.2005; 12(4):223-229.
9. Jemal A, Murray T, Ward E, et al. Cancer statistics, 2005. CA Cancer J Clin. 2005; 55:10-29.
10. Jonathan B. Heistein, MD, Robert L. Ruberg, MD. Melanoma.2012,may 16.
11. Jose M Pimiento, Eillen M Larkin, Keiran SM Smalley et al. Melanoma gnotypes and fenotypes get personal. Lab Invest.2013; 93(8):858-867.

12. Lens MB, Dawes M. Global perspective of contemporany epidemiological trends of cutaneous malignant melanoma. Br J Dermatol.2004; 150:179-85.
13. Muresan Andrei Mihai. Skin Cancer. „Ion Chiricuta" Oncology Institute 2007.
14. N.Bories, S.Dalle, S.Debarbieux, et al. The British Journal of Dermatology.2008;158(6):1224-1229.
15. Richard Danialan, Arun Gopinath, Amanda Phelps, Michael Murphy, Jane M Grant-Kels. Accurate identification of melanoma tumor margins. Expert Rev Dermatol. 2012; 7(4): 343-358.
16. Thomas B. Fitzpatrick, Klaus Wolff, Richard Allen Johnson, Dick Suurmond: Fitzpatrick's, Color Atlas & Synopsis of Clinical Dermatology, Fifth Edition,2005
17. Wachsmuth RC, Turner F, Barett JH, et al. The effect of sun exposure in determining nevus density in UK adolescent twins. J Invest Dermatol.2005;124:56-62.