CASE REPORTS

RJME
Romanian Journal of Morphology & Embryology
http://www.rjme.ro/

Basal cell carcinoma miming cutaneous melanoma

INA RUXANDRA PETRESCU[1)], MARIA SAJIN[2)], MARIANA COSTACHE[2)], G. SIMION[3)]

[1)]*Department of Plastic Surgery and Reconstructive Microsurgery, Emergency University Hospital, Bucharest*
[2)]*"Carol Davila" University of Medicine and Pharmacy, Bucharest*
[3)]*Department of Pathology, Emergency University Hospital, Bucharest*

Abstract

In the last decades, the incidence of skin cancer is in continuous growth, but the mortality remains at the same level thanks to the new imaging diagnosis methods and surgical treatment. A real problem regarding differential diagnosis between cutaneous melanoma and non-melanotic skin tumor appear, despite advanced technologies, which have a major impact on treatment management. We reported two cases with clinical and dermoscopic aspects of cutaneous melanoma, sustained by positive lymphoscintigraphy. The histopathological exams established that the skin tumor was a pigmented basal cell carcinoma. In such difficult cases, the accuracy of diagnosis is certificated only by the microscopical examination with clinical, treatment and prognosis changes.

Keywords: cutaneous melanoma, basal cell carcinoma, sentinel lymph node biopsy, lymphoscintigraphy, surgical treatment.

Introduction

Cutaneous melanoma represent about 4% of skin cancer cases and is responsible for 90% of skin cancer deaths and incidence have been rising in past 30 years (1975–2005): from 8 to 22 cases/100 000/year in males and from 7 to 15 cases/100 000/year in females – numeric values for United States, according to the *American Cancer Society*. In Romania, the mortality due to the skin cancer in men and women age 20–44 years in periods 1985–1989 and 1995–1999 has a favorable trends for male: 0.87 to 0.85 and downward trends for women: 0.67 to 0.84. At the age 45 to 64 years, it records unfavorable trends both in male: 4.18 to 5.02 and in women: 2.29 to 2.73 [1].

Clinical diagnosis is positive in 60% of cases and includes a few clinical subtypes: superficial spreading melanoma lentigo maligna melanoma, nodular melanoma, acral lentiginous melanoma, mucosal lentiginous melanoma, amelanotic melanoma [2]. Imaging diagnosis protocol includes: dermoscopy and computed dermoscopy, chest X-ray, computer tomography (CT), magnetic resonance imaging (MRI), sentinel lymph node biopsy (SLNB), positron-emission tomography (PET) and positron-emission tomography and computed tomography (PET/CT) [3].

Basal cell carcinoma

The most frequently skin tumor is aggressive by its local invasive potential and recurrence, but very infrequent metastases (0.5%). The incidence of basal cell carcinoma is also increasing in the last period at more than 10% in white population. Elderly population is more affected [4].

Typical clinical aspect is represented by the rodent ulcer with central ulceration and indurated borders and strong potential of deep tissue penetration, located especially on the head and neck (80%). Superficial basal cell carcinoma is a flat erythematous lesion on the trunk, with slow development. Nodulocystic clinical subtype is presented as a unique red nodule with a dilated network of vessel for elective on the face. The morphoeic basal cell carcinoma is considered the most aggressive form with ill-defined margins and large volume. The pigmented clinical subtype must to be differentiated from cutaneous melanoma.

Patients, Methods and Results

Tissue specimens were processed according conventional histopathological techniques, including paraffin, 3 μm section stained by Hematoxylin–Eosin (HE) in Department of Pathology of Emergency University Hospital of Bucharest.

Case No. 1

N.I., male, 54-year-old, with relative short term history (5 month) of pigmented lesion at the left mandibular region was presented in clinic after a dermatological consultation including and dermoscopy with presumptive diagnosis of ulcerated cutaneous melanoma (Figure 1) and a positive lymphoscintigraphy (Figure 2). Clinical aspect of tumor was represented by a pigmented ulcerated lesion of 2 cm diameter, with irregular borders and inflammatory reaction at the inferior border, located at submandibulary region. Tumor was indurated, painless, infiltrated the surrounded tissue and also it was presented homolateral submandi-

bulary adenopathy. Preoperative, 1 mL of Vital Blue Dye was injected intradermally to help the lymph node mapping. Surgical treatment under general anesthesia consists in lesion excision with safety margins (Figure 3) and lymph nodes removal (Figure 4).

Histopathological exam revealed basaloid cells proliferation with peripheral palisading, with a few mitoses, hyperchromic nuclei, with small amount of cytoplasm, intra- and extracellular melanic pigment and disposed in nests separated by fine fibrovascular stroma. The tumor infiltrated papillary dermis, yet well-defined limits. The lymph node presented hyperplasic lymphoid follicles and sinusal histiocytosis (Figure 7). Final diagnosis established that skin lesion was pigmented basal cell carcinoma (Figures 5 and 6).

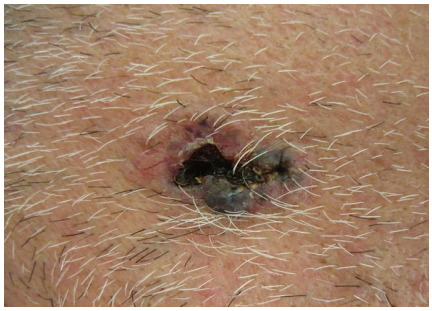

Figure 1 – ***Case No. 1: macroscopic aspect of pigmented basal cell carcinoma at the mandibular region.***

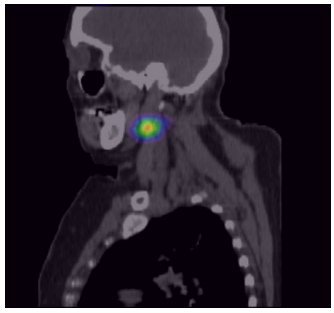

Figure 2 – ***Case No. 1: lymphoscintigraphy, positive sentinel lymph node.***

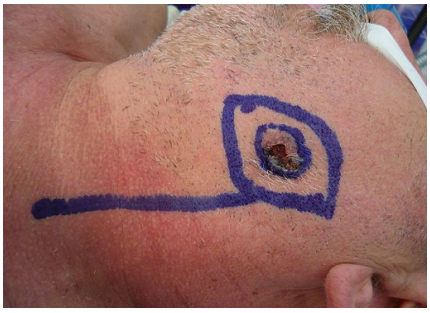

Figure 3 – ***Case No. 1: operative detail.***

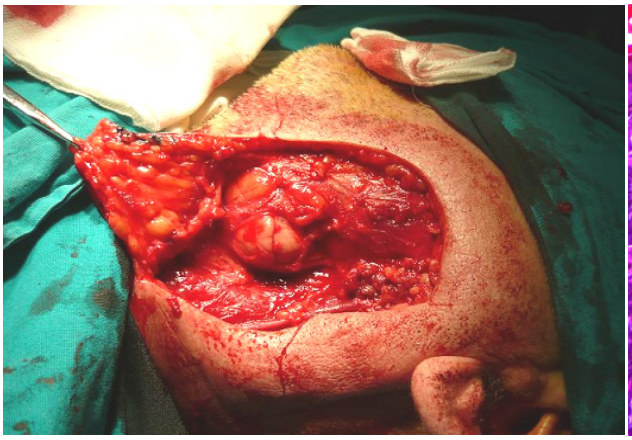

Figure 4 – ***Case No. 1: operative detail.***

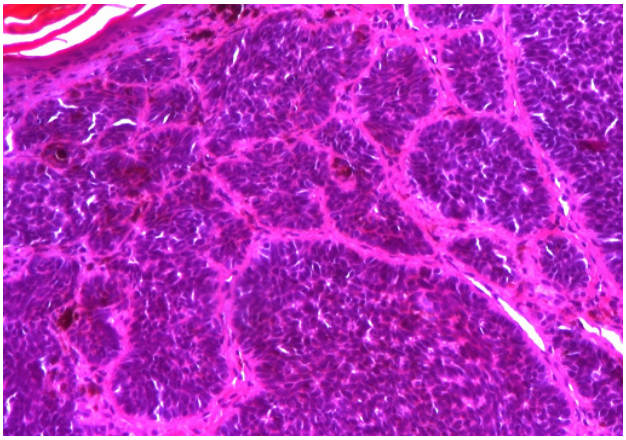

Figure 5 – ***Case No. 1: microscopic aspect of pigmented basal cell carcinoma (HE stain, ×200).***

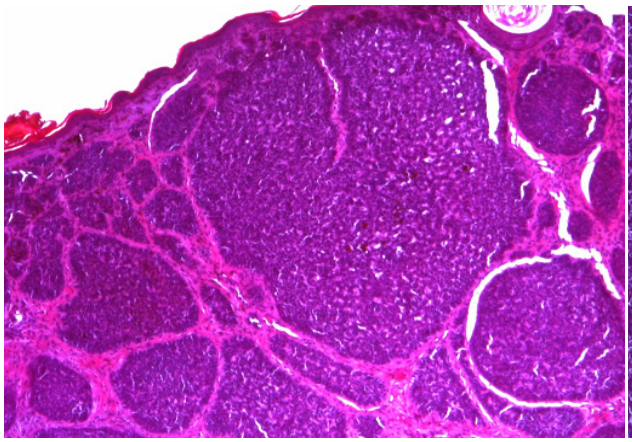

Figure 6 – ***Case No. 1: microscopic aspect of pigmented basal cell carcinoma (HE stain, ×40).***

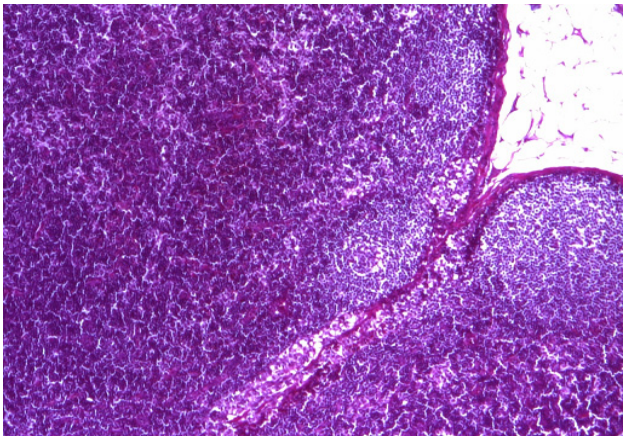

Figure 7 – ***Case No. 1: microscopic aspect of lymph node without tumor cells, only sinusal histiocytosis (HE stain, ×100).***

Case No. 2

P.C., male, 41-year-old, with relative long term (3 years) history of pigmented lesion on left laterothorax also with a positive dermoscopy was hospitalized in Plastic Surgery Department with presumptive diagnosis of superficial spreading cutaneous melanoma (Figure 8). The clinical aspect of tumor was represented by a flat erythematosus lesion, of 4 cm diameter, with irregular border, with isolated vesicles and multiple small ulceration, with peripheral pigmented zones. Tumor

palpation revealed a soft, painless, superficial lesion. Local and regional lymph node could not be detected at clinically exam. The lymphoscintigraphy performed in order to detect sentinel lymph node was positive for anterior axillary lymph nodes (Figure 9). The cranio-cerebral and abdominal computer tomographies revealed absences of metastases while chest computer tomography found suspect mediastinum adenopathy. The level of S100 protein was in normal limits: 0.075 µg/L. Before operation, it was injected intra-dermally 1 mL of Vital Blue Dye to facilitate the identification of metastatic lymph nodes (Figure 10). Surgical treatment under general anesthesia consists in tumor excision with large limits (2.5–3 cm) in subfascial plane and axillary lymph nodes excision (Figure 11). During surgery, we found that the presumptive sentinel lymph node was enlarged, about 2 cm, but did not retain the blue dye. Histopathological aspects were represented by the basaloid, hyperchromic cells arranged in irregular nests, with a little melanic pigment and prominent fibrovascular stroma and young fibroblasts. Lymph node presented follicular hyperplasia and sinusal histiocytosis (Figure 14). Final diagnosis was basal cell carcinoma, pigmented subtype (Figures 12 and 13).

Two cases with pigmented skin tumor, which had a presumptive dermoscopic diagnosis of cutaneous melanoma and positive lymphoscintigraphy, were invalidating by the histopathological exam.

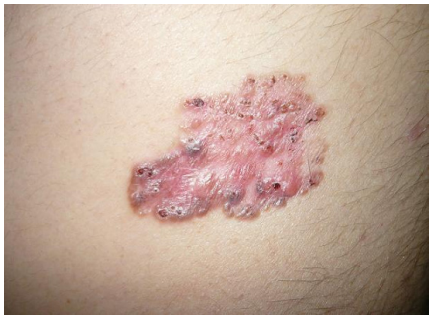

Figure 8 – ***Case No. 2: macroscopic aspect of laterothoracic pigmented basal cell carcinoma.***

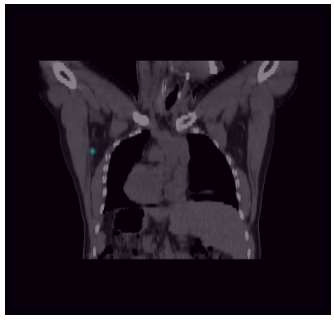

Figure 9 – ***Case No. 2: lymphoscintigraphy with positive anterior axillary sentinel lymph node.***

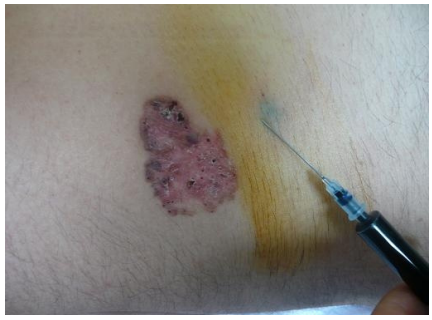

Figure 10 – ***Case No. 2: the Vital Blue Dye intradermally injection.***

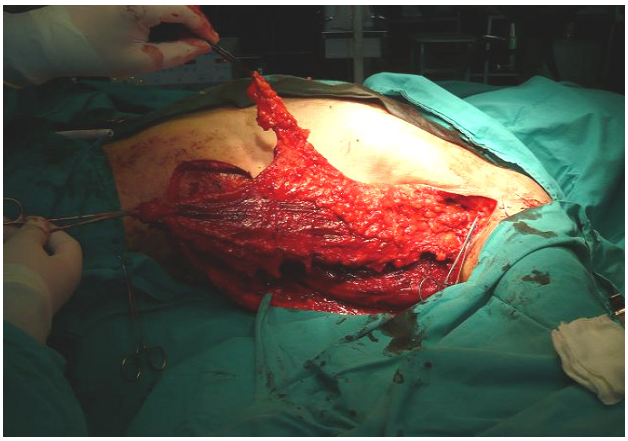

Figure 11 – ***Case No. 2: operative details with axillary lymph node dissection.***

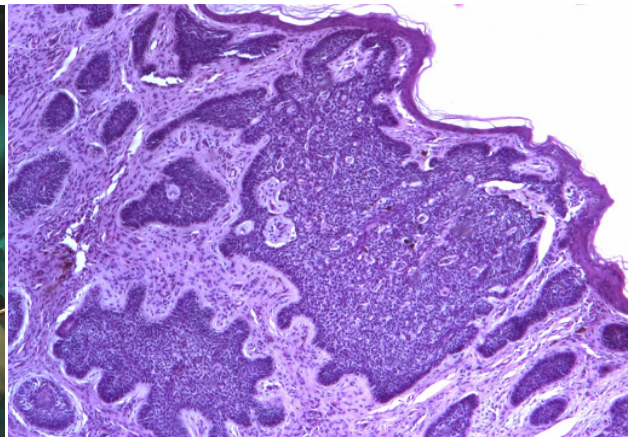

Figure 12 – ***Case No. 2: microscopic aspect of pigmented basal cell carcinoma (HE stain, ×40).***

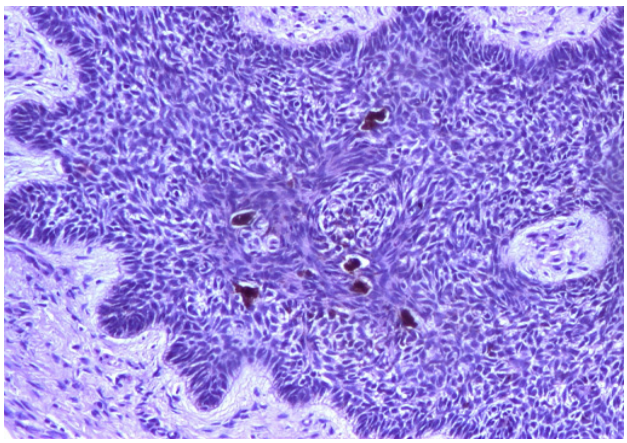

Figure 13 – ***Case No. 2: microscopic aspect of pigmented basal cell carcinoma (HE stain, ×200).***

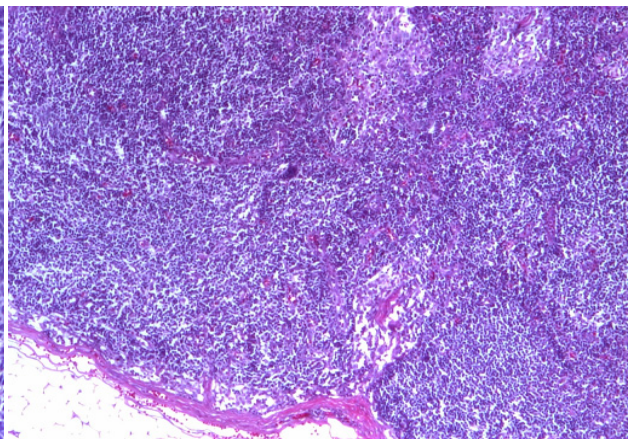

Figure 14 – ***Case No. 2: microscopic aspect of lymph node with sinusal histiocytosis (HE stain, ×100).***

Discussion

Superficial spreading melanoma, the most frequent form, accounts 70% of total melanomas presented like a an irregular and different color (dark-brown, red, white, black) macula on the trunk in man and lower extremities in women. Nodular melanoma represents 15% of melanomas and is generally localized on the trunk with clinical aspect of a blue-black nodule, which can be ulcerated. Lentigo maligna melanoma accounts for 5% of melanoma and appear on sun damaged skin areas, on a precursor lesion: lentigo maligna. Clinically, it presents asymmetrical wide spread pigmented macula which grow slowly in few years. The main feature of this clinical subtype is prolonged horizontal development of melanoma *in situ* and so that an important number of cases have a good prognostic after surgical excision.

Dermoscopy offers a 10–20-fold magnification, and detected the early stage cutaneous melanoma, and in the latest year's dermoscopy prove a very useful non-invasive and cheap technique for pigmented skin lesion and due to the pattern analysis can made the differential diagnosis between benign melanocyte tumors and melanoma [5].

Dermoscopy is the imaging technique, which change radically melanoma prognosis thanks to the early detection of lesion when melanoma is curative. Even dermoscopy improved melanoma diagnosis, still exist false-positive results.

Dermoscopy should provide differential diagnosis between pigmented basal cell carcinoma and other suspicious pigmented skin lesion: melanoma, dysplastic nevi blue nevus, congenital melanocytic nevus, melanoma arising on congenital nevi or xeroderma pigmentosum.

In 2008, Menzies SW *et al.* demonstrated a sensitivity of 70% and specificity of 56% of differential diagnosis of cutaneous melanomas from all non-melanoma tumors [6].

Histopathology of basal cell carcinoma presents multiple variants: nodular, superficial, micronodular, infiltrating, basosquamos, fibroepithelial, cystic, infundibulocystic, adenoid, sclerosing/morphoeic, pigmented, keratotic, with adnexal differentiation neuroendocrine, schwannoid or clear cell subtype.

Pigmented basal cell carcinoma represents a clinical form which macroscopic and dermoscopic features mimic (due to the melanic pigment) malignant melanoma. The pigment is stored intracellular in isolated or grouped melanocytes and in stomal melanophages. Yet the other listed basal cell forms can present small quantity of pigment. Histological basal cell carcinoma presents small size tumor cells, monomorphic, with mitoses, but without pleomorphism, while melanoma presents medium/large tumor cells with pleomorphism, mitoses and infiltrating aspect. Melanoma subtype with small cells can creates some diagnosis problems and in these cases immunohistochemical tests clarify final diagnosis. So, basal cell carcinoma is BerEP4 positive and S100 negative, while melanoma is BerEP4 negative and S100, MART-1, HMB45 positive. Melanoma with small cells must be differentiated from Merkel cell carcinoma, which is BerEP4 positive, CD20 positive and S100 negative.

Sentinel lymph node biopsy (SLNB), as proposed initially by Morton DL *et al*., is actually the gold standard for melanoma investigation and is included in AJCC classification. The first station of lymph drainage tumor is in sentinel node, so that the probability to be the first metastatic site is maxim. Biopsy of SLN is followed by histopathological examination. This method is indicated in patients with intermediate-risk: lesion thickness of 1–4 mm and high-risk lesion >4 mm. Pre-operative lymphoscintigraphy is an important step for detection sentinel lymph node biopsy and increased the accuracy of the investigation at 95–99%. This technique is the most accurate method for micrometastases ≤4mm, despite the adverse effects, like radiation exposure or potential local complication (lymphedema). Vital blue dye is injected peritumoral for intraoperative visualization of sentinel lymph node and is easy, inexpensive and helpful procedure. SLNB became a standard in melanoma staging and is important for treatment decision, mostly adjuvant schedules. A positive result is followed by elective lymph node dissection [7].

Biopsy of sentinel lymph node is a very useful in melanoma staging and a strong predictable factor. Estourgie SH *et al*. on a group of 250 melanomas found only 24% sentinel node-positive and 9% false negative rate, which is very high [8]. Vital Blue Dye injected intradermally helps the lymph nodes mapping. The accuracy of lymphoscintigraphy in sentinel lymph node diagnosis is a problem to debate. The technique has 95% specificity. Gershenwald JE and Filder IJ, in a clinical study with 520 melanoma patients, found a 5.2% false negative rate. The question regards false positive results can receives response in ability of inflammatory lymph node to retain the radiocolloid [9].

Additionally, serological biomarkers like LDH, S100, C-reactive protein, MIA (melanoma inhibitory activity protein), TA90 (tumor-associated antigen 90 immune complexes), IL6. A combination of serum biomarkers correlated with AJCC staging, play an important prognostic role, very useful in latest melanoma stages, monitoring after surgical excision of primary tumor in I–III stages and evaluation therapy in advanced stages. But, there are two principal limits: none a single marker can be considered specific for melanoma and predictive significance are just for latest stages: presence of metastases or good therapy response, not for early stages [10].

The excisional biopsy of a skin tumor is considered the safety way comparative with incisional or punch biopsy since the first method can avoid inaccurate tumor thickness measurements. Martin RC *et al.*, in 2005, on a large clinical trial of 2164 patients reported no significant difference between three methods of biopsy (excisional, incisional and shave) regarding local or distant recurrence and to increase the risk of sentinel lymph node micrometastases. He demonstrated on a group of 265 samples incisional biopsy with 496 control melanomas that melanoma prognoses and the risk of recurrences are not affected [11]. In difficult cases like nevoid or desmoplastic melanomas, incisional biopsy

offers less accuracy of diagnosis. Also in melanoma cases, arising from nevus this technique can ensure a benign sample with severe implication on final diagnosis. In cases when surgical treatment is the unique indication, two operations – biopsy and excision of lesion can avoided and the excisional biopsy seems to be the best option.

Karimipour DJ *et al.* found that 21% of 1783 melanoma patients were upstaged thanks to partial biopsy method [12].

Surgical excision of primary cutaneous melanoma is certain method of treatment, always under general anesthesia. An adequate limit of surgical excision was established by the *WHO Melanoma Group*, which performed large randomized study, which proved that the disease free period was similar for 1 cm margins of excision primary melanoma of 2 mm thickness likewise 3 cm borders. Also, some recent studies recommended safety margins: 0.5 cm for *in situ* tumor, 1 cm for ≤2 mm tumor thickness and 2 cm for >2 mm tumor thickness. If 1 cm limits of excision are safety, remain an unsolved problem because the presence of cell nests closely to the primary tumor [13]. Lymph node dissection is performed in cases with micro- and macro-metastases mapped by the SLNB. Mohs micrographic surgery proved that is a very helpful method in non-melanoma skin malignancies grace to the entire margins of tumor are examined and play an important role in melanoma management particularly ill-define lesion. The aim of this technique is to evaluate the entire tumor border and the deep. Excised lesion is histopathological analyzed. If remain tumor tissue the procedure is repeated. This treatment of melanoma technique is more laborious, but recent studies has shown that use of immunostains (especially MART-1) of frozen section improve the results [14].

Conclusions

Pigmented basal cell carcinoma may pose differential diagnosis problems with cutaneous melanoma. Imagistic diagnosis including dermoscopy and lymphoscintigraphy offer misinterpreted results and it is necessary to improve the quality of this methods. The tumor biopsy in this difficult cases is better to change with excisional biopsy of lesion in safety margins, followed by the intraoperative histological exam is the best option. Thereby the surgical procedure is limited just to the tumor excision not and the lymph nodes dissection. So that the short and long-term consequences of a large operation like lymphoreea and lymphedema are avoided. False positive imaging results determine in described cases an overvaluation and implicitly a complex operations. Final diagnosis in these difficult cases was proved by histopathological exam and immunohisto-chemical tests.

References

[1] Bosetti C, La Vecchia C, Naldi L, Lucchini F, Negri E, Levi F, *Mortality from cutaneous malignant melanoma in Europe. Has the epidemic leveled off?* Melanoma Res, 2004, 14(4):301–309.

[2] Zalaudek I, Ferrara G, Argenziano G, Ruocco V, Soyer HP, *Diagnosis and treatment of cutaneous melanoma: a practical guide*, Skinmed, 2003, 2(1):20–31; quiz 32–33.

[3] Garbe C, Eigentler TK, *Diagnosis and treatment of cutaneous melanoma: state of the art 2006*, Melanoma Res, 2007, 17(2):117–127.

[4] Wong CSM, Strange RC, Lear JT, *Basal cell carcinoma*, BMJ, 2003, 327(7418):794–798.

[5] Dancey AL, Mahon BS, Rayatt SS, *A review of diagnostic imaging in melanoma*, J Plast Reconstr Aesthet Surg, 2008, 61(11):1275–1283.

[6] Menzies SW, Kreusch J, Byth K, Pizzichetta MA, Marghoob A, Braun R, Malvehy J, Puig S, Argenziano G, Zalaudek I, Rabinovitz HS, Oliviero M, Cabo H, Ahlgrimm-Siess V, Avramidis M, Guitera P, Soyer HP, Ghigliotti G, Tanaka M, Perusquia AM, Pagnanelli G, Bono R, Thomas L, Pellacani G, Langford D, Piccolo D, Terstappen K, Stanganelli I, Llambrich A, Johr R, *Dermoscopic evaluation of amelanotic and hypomelanotic melanoma*, Arch Dermatol, 2008, 144(9):1120–1127.

[7] Morton DL, Wen DR, Wong JH, Economou JS, Cagle LA, Storm FK, Foshag LJ, Cochran AJ, *Technical details of intraoperative lymphatic mapping for early stage melanoma*, Arch Surg, 1992, 127(4):392–399.

[8] Estourgie SH, Nieweg OE, Valdés Olmos RA, Hoefnagel CA, Kroon BB, *Review and evaluation of sentinel node procedures in 250 melanoma patients with a median follow-up of 6 years*, Ann Surg Oncol, 2003, 10(6):681–688.

[9] Gershenwald JE, Fidler IJ, *Cancer. Targeting lymphatic metastasis*, Science, 2002, 296(5574):1811–1812.

[10] Mouawad R, Spano JP, Khayat D, *Old and new serological biomarkers in melanoma: where we are in 2009*, Melanoma Res, 2010, 20(2):67–76

[11] Martin RC 2nd, Scoggins CR, Ross MI, Reintgen DS, Noyes RD, Edwards MJ, McMasters KM, *Is incisional biopsy melanoma harmful of?* Am J Surg, 2005, 190(6):913–917.

[12] Karimipour DJ, Schwartz JL, Wang TS, Bichakjian CK, Orringer JS, King AL, Huang CC, Johnson TM, *Microstaging accuracy after subtotal incisional biopsy of cutaneous melanoma*, J Am Acad Dermatol, 2005, 52(5):798–802.

[13] Rutkowski P, Zdzienicki M, Nowecki ZI, van Akkooi ACJ, *Surgery of primary melanomas*, Cancers, 2010, 2(2):824–841.

[14] Whalen J, Leone D, *Mohs micrographic surgery for the treatment of malignant melanoma*, Clin Dermatol, 2009, 27(6):597–602.

Corresponding author

Ina Ruxandra Petrescu, MD, Department of Plastic Surgery and Reconstructive Microsurgery, University Emergency Hospital Bucharest, 169 Splaiul Independenței Avenue, 050098 Bucharest, Romania; Phone +40722–556 838, e-mail: inapetrescu@yahoo.com

Received: June 25th, 2010 *Accepted: February 26th, 2011*