Sentinel Lymph Node in Thin and Thick Melanoma

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The recommendation for sentinel lymph node biopsy (SLNB) is a controversial problem in the management of cutaneous malignant melanoma (CMM). Rovere et al. performed a study with the objective to assess the epidemiologic profile of patients with CMM, who underwent SLNB in Blumenau-Santa Caterina region in Brazil [1]. According to *ESMO Clinical Practice Guidelines* for diagnosis, treatment and follow-up of CMM, the authors wrote that SLNB is recommended for CMM with thickness > 1 mm. Rovere et al. concluded that Breslow thickness, ulceration, nodular subtype, Clark's level IV are associated with SLNB status [1]. We believe that recommendations for SLNB should reflect the biological concept of CMM evolution. The histogenetic theory considers two steps of CMM progression – the radial growth phase (RGP) and vertical growth phase (VGP), with the exception of nodular CMM lacking RGP [2–4]. Two sub-categories of RGP are recognized – the intra-epidermal RGP (*in situ* melanoma) and the micro-invasive RGP. The former is characterized by proliferation of malignant, transformed melanocytes above the basement membrane (Clark's level I), with pagetoid or lentiginous morphologic pattern. The latter shows invasion into the papillary dermis (Clark's level II or III), with presence of single cells or small nests, in absence of tumor nodule or papule. The dermal nests are invariably smaller than the junctional ones, while the cytological appearance of the junctional and dermal component is overlapping. The absence of dermal mitoses is an absolute criterion; in fact, micro-invasive RGP lacks metastatic potential [2–4]. However, according to our observations, metastases may be found in 1–2% of micro-invasive RGPs, when they are associated with significant regression (> 75%; > 0.75 mm in depth). Therefore, it is likely that this regression may incorporate melanoma cells able to metastasize, with metastases prior the occurrence of regression [5]. VGP designates the point at which CMM becomes biologically capable of producing metastatic events. The tumor infiltrates as nodules of malignant melanocytes, filling the superficial papillary dermis with tendency for deep

Tab. 1. The malignant melanocytic lesions of the skin can be subdivided, according to the Breslow thickness, in thin melanoma (≤ 1 mm) or thick melanoma (> 1 mm).

The intra-epidermal radial growth phase and the micro-invasive radial growth phase without regression of thin melanoma are devoid of tumorigenic potential, while the micro-invasive radial growth phase with regression is burdened by an uncertain metastatic potential (at diagnosis). The early invasive vertical growth phase of thin melanoma and the subcategories of invasive vertical growth phase of thick melanoma show all tumorigenic potential, directly correlated to the depth of invasion and mitogenicity (pTis, pT1, pT2, pT3, pT4 and a/b specifications are adapted from the AJCC staging system).

Thin melanoma **Breslow thickness ≤ 1 mm**	**Thick melanoma** **Breslow thickness > 1 mm**
intra-epidermal radial growth phase (*in situ*, **pTis**)	invasive vertical growth phase > 1 mm ≤ 2 mm (**pT2**)
micro-invasive radial growth phase without regression (**pT1**)	invasive vertical growth phase > 2 mm ≤ 3 mm (**pT3**)
micro-invasive radial growth phase with regression (**pT1**)	invasive vertical growth phase > 3 mm ≤ 4 mm (**pT3**)
early (≤ 1 mm) invasive vertical growth phase (**pT1**)	invasive vertical growth phase > 4 mm (**pT4**)

a and b specifications are assigned based on ulceration and number of mitoses for mm^2
a – without ulceration and mitoses < $1/mm^2$
b – with ulceration or mitoses ≥ $1/mm^2$

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invasion into reticular dermis (Clark's level IV) and subcutaneous tissue (Clark's level V) [2–4]. For definition, VGP includes the properties of ‚tumorigenicity' and ‚mitogenicity' [2–4]. Because of the increasing frequency of thin melanomas, there is a great need to develop more refined predictors of SLNB. Today, the scientific community is focusing on the clinical significance of different histological subtypes of thin melanoma [6]. In fact, there is a subset of patients affected by thin melanoma, who develop nodal or distant metastases with worse prognosis [7]. From our experience, as reported in Tab. 1, thin melanoma can be categorized in the following four histological subtypes: I. the intra-epidermal RGP; II. the non-tumorigenic micro-invasive RGP without regression; III. the micro-invasive RGP with regression of uncertain tumorigenic potential; IV. the tumorigenic early invasive VGP [8]. In micro-invasive RGP with regression and in all cases of VGP, including the early invasive VGP of thin (≤ 1 mm) melanoma (pT1) and the invasive VGP of thick (> 1 mm) melanoma (pT2, pT3, pT4), the SNLB should be performed, independently from other risk factors, because the tumor has the potential to metastasize.

References

1. Rovere RK, Silva de Lima A, DeMarchi V et al. Sentinel lymph node in melanoma – a study conducted in the south of Brazil. Klin Onkol 2016; 29(4): 274–278. doi: 10.14735/amko2016274.

2. Pusiol T, Piscioli F, Speziali L et al. Clinical Features, dermoscopic patterns, and histological diagnostic model for melanocytic tumors of uncertain malignant potential (MELTUMP). Acta Dermatovenerol Croat 2015; 23(3): 185–194.

3. Piscioli F, Pusiol T, Roncati L. Diagnostic approach to melanocytic lesion of unknown malignant potential. Melanoma Res 2016; 26(1): 91–92. doi: 10.1097/CMR.0000000000000215.

4. Piscioli F, Pusiol T, Roncati L. Diagnostic disputes regarding atypical melanocytic lesions can be solved by using the term MELTUMP. Turk Patoloji Derg 2016; 32(1): 63–64. doi: 10.5146/tjpath.2015.01330.

5. Piscioli F, Pusiol T, Roncati L. Histopathological determination of thin melanomas at risk for metastasis. Melanoma Res. In press 2016. doi: 10.1097/CMR.0000000000000288.

6. Piscioli F, Pusiol T, Roncati L. Nowadays a histological subtyping of thin melanoma is demanded for a proper patient management. J Plast Reconstr Aesthet Surg. In press 2016. pii: S1748-6815(16)30236-4. doi: 10.1016/j.bjps.2016.08.026.

7. Piscioli F, Pusiol T, Roncati L. Choosing wisely the patients affected by thin melanoma to be submitted for sentinel lymph node biopsy. J Am Acad Dermatol. In press 2016.

8. Piscioli F, Pusiol T, Roncati L. Thin melanoma subtyping fits well with the American Joint Committee on Cancer staging system. Melanoma Res. In press 2016. doi: 10.1097/CMR.0000000000000301.

Imunologická sekce ČOS

Na jaře 2016 se uskutečnily volby do výboru Imunologické sekce České onkologické společnosti (ČOS). Do výboru byli zvoleni prim. MUDr. Ivana Krajsová, MBA (Dermatovenerologická klinika 1. LF UK a VFN v Praze), doc. MUDr. Tomáš Büchler, Ph.D. (Onkologická klinika 1. LF UK a Thomayerova nemocnice, Praha), prof. MUDr. Pavel Dundr, Ph.D. (Ústav patologie, 1. LF UK a VFN v Praze), prof. MUDr. Aleš Ryška, Ph.D. (Fingerlandův ústav patologie, LF UK a FN Hradec Králové), prof. MUDr. Bohuslav Melichar, Ph.D. (Onkologická klinika LF UP a FN Olomouc), MUDr. Alexandr Poprach, Ph.D. (Klinika komplexní onkologické péče, MOÚ, Brno), prof. MUDr. Luboš Petruželka, CSc. (Onkologická klinika 1. LF UK a VFN v Praze), PharmDr. Irena Netíková, Ph.D. (Oddělení klinické farmakologie a farmacie, 1. LF UK a VFN v Praze) a MUDr. Eugen Kubala (Klinika onkologie a radioterapie LF UK a FN Hradec Králové).

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V naší další činnosti budeme na tyto aktivity navazovat. Příchod nových imunologických léků do každodenní klinické praxe přináší nové problémy a výzvy. Zatímco o účinnosti nových imunologických léků není již nutné nikoho přesvědčovat, zvládání jejich nežádoucích účinků a otázky zavádění pozitivních a negativních prediktivních markerů pro výběr pacientů si určitě budou vyžadovat hodně přemýšlení a práce. Právě v optimalizaci využití nových metod imunoterapie k prospěchu nemocných vidím prioritu pro nový výbor.

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