

Lentigo Maligna Melanoma – the Review

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ABSTRACT

Lentigo maligna melanoma (LMM) is a slowly growing tumor of elderly white population. It typically develops on chronically sun-exposed skin of the head and neck area which indicates that the cumulative exposure to the UV radiation has crucial role in the development of LMM. Precursor lesion is lentigo maligna (LM) which commonly presents as an irregular brownish pigmented macular lesion persisting for years. Women are affected more often as men by LMM, with the average age of over 60 years. The age of onset has dropped over the past years and this tumour is nowadays also diagnosed in 40-year-old individuals. However, the incidence rate increases with age and peaks in the seventh and eighth decades of life. The prognosis for invasive lentigo maligna melanoma does not differ from that for other histogenetic types of melanoma after controlling for tumour thickness. The diagnosis and treatment of LMM remain challenging. In this presentation, we review the epidemiology, clinical presentation, histopathology, and treatment of LMM.

Key words: *lentigo malignant melanoma, lentigo maligna*

Cutaneous melanoma is one of the most aggressive tumors in dermatology¹. The incidence has increased dramatically in all parts of the world over the past 30 years and shows little sign of leveling off². The incidence in Croatia is not exceptional. In the past 40 years in Croatia the incidence of melanoma is also in rise for more than 300%³. Women and men are almost equally affected. In the last decades, melanoma often occur in relatively younger people, between the age of 25 and 40, rarely in the childhood. In 2006. i 2007. there were 60,000–62,000 new cases of invasive tumor and aprox. 48,000 in situ melanoma. However, survival in patients with melanoma in Western European countries has increased markedly in recent years, due to timely recognition of the disease, as melanoma is curable by means of surgical excision if diagnosed in early stages of the disease⁴. Unfortunately, in Croatia the mortality remains higher even though the incidence is lower than those in some Western European countries

Melanoma is classified into 4 main subtypes; superficial spreading (70%), nodular (10–15%), and acral lentiginous melanoma (5%) and lentigo malignant melanoma (5–15 %).¹ Lentigo maligna (LM) is a subtype of melanoma in-situ. Most authors refer to this lesion as

LM when it is confined to the epidermis, and as lentigo malignant melanoma (LMM) when it invades the dermis.

Epidemiological data

Many authors consider lentigo maligna to be a pre-invasive lesion induced by long-term cumulative ultraviolet injury. It is supported by the fact that its incidence is the highest in Hawaii island, and the lowest in Scandinavian region; the region that has lower ultraviolet index. The annual incidence of LM in Australia was estimated at 1.3: 100.000⁷.

We represent data³ from Croatian Referral Center for Malignant melanoma. From 2002–2008 there were 974 patients with melanoma and for 590 patients we knew the histology subtype. 35 patients had Lentigo maligna melanoma which is 5.9 %. The percentage correlates with Western European countries data. Women slightly predominated; 20 women versus 15 men. Generally, patients with lentigo maligna are older than 40 years, with a mean age of 65 years. The peak incidence occurs in the seventh to eighth decades of life.

Clinical presentation

Lentigo maligna usually develops on chronically sun-exposed skin of the head and neck, with a predilection for the cheek¹. In men, it is more often on the left side of the cheek (drivers side) while as in the women it is on the right side (passenger's side)⁸. A plausible explanation for this phenomenon is that, according to the Australian road traffic accident database, most Australian drivers are men, and most front seat passengers are women. Lentigo maligna presents as a slowly enlarging tan-to-brown macule with ill-defined borders that expands centrifugally with variable shades of tan, brown, dark brown or black. The lesion often contains net-like black pigmentation. If darker papule or nodule arises or if the skin markings are destroyed, then lentigo maligna melanoma is developing. Lentigo maligna is usually presented 10 to 15 years before progression to lentigo maligna melanoma, but several cases observed rapid progression. The exact percentage of LM cases

that progress to LMM is unknown. Weinstock and Sober estimated an approximate 5% lifetime risk of LMM in patients diagnosed with LM at age 45. However, in two series of 85

LM excisions, more than 50% contained occult invasive foci of melanoma, and, in a more recent report of 92 consecutive cases, 16% of LM lesions undergoing staged excisions harbored unexpected foci of invasion⁹.

Clinically, the main differential diagnosis includes solar lentigo, pigmented actinic keratosis, and seborrheic keratosis¹.

Diagnosis

The most ideal method is excisional biopsy but as these lesions are sometimes quite large, the punch biopsies or incisional biopsy in full thickness are optional, although it is very easy to miss the invasive foci¹⁰. The one should clinical search for more pigmented or slightly elevated parts of the lesion. It is recommended that biopsy is read by pathologist experienced in pigmented lesion.

Although the best diagnostical method is pathological analysis, dermatoscopy can also be helpful¹¹.

Histopathology

Lentigo maligna prototype of horizontal phase of melanoma. When atypical melanocytes begin to grow down into the dermis, the vertical growth phase has begun, representing lentigo maligna melanoma. The hallmark of lentigo maligna is the proliferation of the atypical melanocytes in the epidermal basal layer. There is an in-

creased number of clear cells, many of which are large, irregular or polygonal or which may have atypical nuclei. Sometimes nests of these cells may be seen, often located in a free space below the epidermis but not invading the dermis. In addition the epidermis is usually thinned. Some dermatopathologists take the presence of nests as a criterion for the diagnosis of melanoma in situ. In the dermis there is always marked solar elastosis. As it is always difficult to determine borders of a lentigo maligna, monoclonal antibodies such as HMB45 and S100 B may help to identify the melanocytes but cannot assess their biological role¹.

Treatment

Treatment for the lentigo maligna in situ is excisional biopsy and reexcision after the pathological confirmation¹². It offers the lowest recurrence rates. However, not every lesion is suitable for the complete excision and not every patient is candidate for the surgical procedure, there are several non-surgical modalities as an option. The most widely used is cryotherapy of the lesion. There is no standard procedure how it should be done, but some authors recommend a double freeze (30 to 60 s) – thaw cycle. Cryotherapy may be given with or without local anesthetic. Healing of cryosurgical wounds usually takes longer than excisional wounds do, and the cosmetic results may vary¹³. The post-treatment area is often dyspigmented, and it may be difficult to know if the lesion was cured or if residual disease remains and may necessitate a biopsy to exclude the recurrence.

The radiation therapy showed very low recurrence rate and cosmetically results were promising. Recently there are several reports about beneficial usage of 5% imiquimod, but this should be considered as experimental before larger studies are made¹⁴.

In the case of lentigo malignant melanoma it is as for every other subtype of melanoma. After the pathological analysis confirmed the diagnosis, the reexcision is done and if the lesion is thicker than 1 millimeter, sentinel biopsy should be performed. Follow up is done according to the stage of the disease.

Conclusion

Lentigo maligna should be the goal of the treatment. The differential diagnosis is wide and expect the knowledge, the experience in pigment lesion is also important. In the head and neck region, the one should be especially alert as there is a large number of lesions that are induced by the ultraviolet rays and it is sometimes difficult to distinguish from each other on the sun-damaged skin.

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LENTIGO MALIGNA MELANOM

SAŽETAK

Lentigo maligni melanom (LMM) je sporo rastući tumor starije dobi, koji pogađa uglavnom bijelu rasu. LMM se gotovo uvijek razvija na predjelima kože kronično izloženim suncu, odnosno u području glave i vrata, ponajprije na nosu i obrazima, što navodi na zaključak da je kumulativan učinak UV zračenja presudan u nastajanju ovog oblika melanoma. Prekursorska promjena – lentigo maligna (LM) očituje se kao nejednoliko smeđa mrlja različita oblika, koja traje godinama. LMM se češće dijagnosticira u žena nego u muškaraca, u prosječnoj dobi od preko 60 godina. Iako je dobna granica u kojoj se dijagnosticira LMM značajno je niža posljednjih godina, te se danas ovaj oblik melanoma može vidjeti i u dobi od 40 godina, još uvijek kod LMM incidencija raste s dobi i najčešće se dijagnosticira u ljudi u sedmom ili osmom desetljeću života. Kao i kod drugih oblika melanoma, debljina tumora predstavlja najvažniji prognostički čimbenik. Dijagnostika i liječenje LMM često predstavljaju klinički izazov. U ovom izlaganju bit će riječ o epidemiologiji, kliničkoj slici, histologiji i liječenju LMM.