Acral Lentiginous Melanoma Diagnosed using Combination of Dermoscopic and Histopathological Examination

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Keywords: melanoma, acral lentiginous, dermoscopy, histopathology

Abstract: Melanoma is a malignant tumor, which arises from melanocyte, and most commonly appears initially on the skin. Melanoma may arise also on mucosal surface even the leptomeningeal. Risk factors for melanoma could come endogenously and exogenously. Melanoma is still one of the leading causes of death by cancer in the world. Acral lentiginous melanoma (ALM) is an uncommon type of melanoma and usually diagnosed in the elderly on the extremities or nails. Clinically acral melanoma may be diagnosed as fungal infection or benign nevus lesion. Dermoscopy has helped clinician in differentiating between benign and malignant nevus lesion, hence not all cases need histopathological examination. Pathognomonic findings in melanoma lesion through dermoscopic examination may assist dermatologist in diagnosing melanoma. Main treatment for melanoma is still wide excision of the lesion and periodic monitoring post excision necessary to evaluate the risk of metastasis and mortality.

1 INTRODUCTION

Melanoma is a malignant tumor of melanocytes that can occur in the skin, mucosa and leptomeningeal. A clinical feature that may resemble ordinary nevus often makes the patient unaware of the condition (Garbe and Bauer, 2012). Epidemiologically melanoma is more commonly found in Fitzpatrick skin type I and II who received excessive sun exposure. In Europe an incidence of 10-25 new cases per 100,000 population is found per year, whereas in the United States 20-30 cases per 100,000 people and the highest in Australia is 50-60 cases per 100,000 population (Garbe and Leiter, 2009; Ferlay et al., 2013). In Indonesia alone the incidence vary but still very low. In RS Dr. M. Djamil Padang found 9 cases of melanoma during 2002-2007 (Azamris, 2011).

Acral lentiginous melanoma (ALM) is a rare type of cutaneous melanoma and is often diagnosed at the later stage with lesions in the palms, soles or inside or around the nails. This condition tends to be found in African and Asian racial groups where rarely found melanoma cases due to excessive sun exposure (Bradford et al., 2009). The way to diagnose melanoma still requires histopathological examination, but with the discovery of dermoscopy has reduced the number of nevus lesions that do not show malignant features (Saida et al., 2011).

The main therapy for melanoma is surgical excision. If there is a sign of metastasis, additional chemotherapy and immunotherapy should be given (Saiag et al., 2007). The following case of acral lentiginous melanoma is diagnosed using combination of dermoscopy and histopathology examination. This case is reported due to a relatively low incidence in Indonesia and to increase understanding of melanoma, diagnosis and appropriate management.

2 CASE

A 53-year-old Balinese mancame to Dermatovenereology polyclinic of Mangunsada Badung Hospital with a chief complaint of dark spot on the right sole of his foot.

Patient has a history oftrauma from a tree thorn 1 year ago and the patient felt that there was a thorn that is embedded in his foot. Patients tried to remove

Santosa, C., Vibriyanti Karna, N., Silayukti, A. and Saputra, H.
Acral Lentiginous Melanoma Diagnosed using Combination of Dermoscopic and Histopathological Examination.
DOI: 10.5220/0008157503630367
In *Proceedings of the 23rd Regional Conference of Dermatology (RCD 2018)*, pages 363-367
ISBN: 978-989-758-494-7

it without any help of medical personnel. About 10 months ago the patient claimed to have black spots appear on the trauma area on his right sole. Patients claimed no pain or itching on that area. The dark spots slowly spread to the adjacent area. History of previous mole on the area is denied. Patients mentioned about awound which appear on the black spots 2 weeks before admission. The patient does not feel any pain on the when being touched.

Patients claimed to have never treated the condition since 1 year ago. History of similar condition in other location was not found. History of malignancy is denied. History of systemic diseases such as hypertension, diabetes mellitus, bleeding disorders are denied by the patient. History of any immunosuppressive conditions was denied. History of similar disease in the patient's family is denied. History of malignancy, asthma, hypertension or diabetes mellitus in patient families is denied. Currentlypatient works as a farmer and often does not use any footwear during work. Patients have no habit of alcohol consumption or smoking.

Physical examination found the general condition of the patient good. Blood pressure 120/80 mmHg, pulse 84x/minute, respiratory frequency 20x/minute and axillary temperature 36.4°C. General status were within normal limit. No enlarged lymph nodes were found. The dermatological status onthe right plantar pedis there are multiple hyperpigmentation macules, well-defined margin, sized 2x3 cm to 5x7 cm with a solitary ulcer above it with rising and regular edge, clean base, round, 1.5 cm in diameter. (**Figure 1A**)

On the investigation using dermoscopy, there are found parallel ridge pattern on the hyperpigmented lesion (**red arrow Figure 1B-D)** andon the ulcer showed blood vessel in dots form (**red arrow Figure 1E**), bluish globule (**asterisk Figure 1E**) and structureless area (**circle Figure 1E**). On the edge of the ulcer there were mass of keratin with a homogeneous black spot on some foci.

Histopathological examination found epidermal layer with a picture of acanthosis accompanied by a thick layer of keratin. There is a proliferation of atypical melanocyte cells along the basal epidermis with disturbed cohesion with relatively large sized morphologies, vacuolized cytoplasm, bizarre nucleus, hyperchromatic, partially with prominent nucleus, and irregular nucleic membrane. These cells contain brownish pigmented granules (melanin). Some of these cells extend along the superficial dermis. Mitosis can be found. The superficial dermis layer looks degenerated and thin. At 1 focus contains necrotic areas with necrotic debris. This fit with the morphological picture of an acral-lentiginous melanoma. (**Figure 2**).

Based on the dermoscopic and histopathological examination, this patient was diagnosed with acral lentiginous melanoma and was performed wide excision of the lesion with a margin of 1 cm and as deep as subcutaneous tissue. The tissue obtained from the excision were examined again and there were clear margin of the lesion. The patient later on got a skin graft from calf area to close the surgical area. The patient was also recommended to do annual check up for the first 5 year.

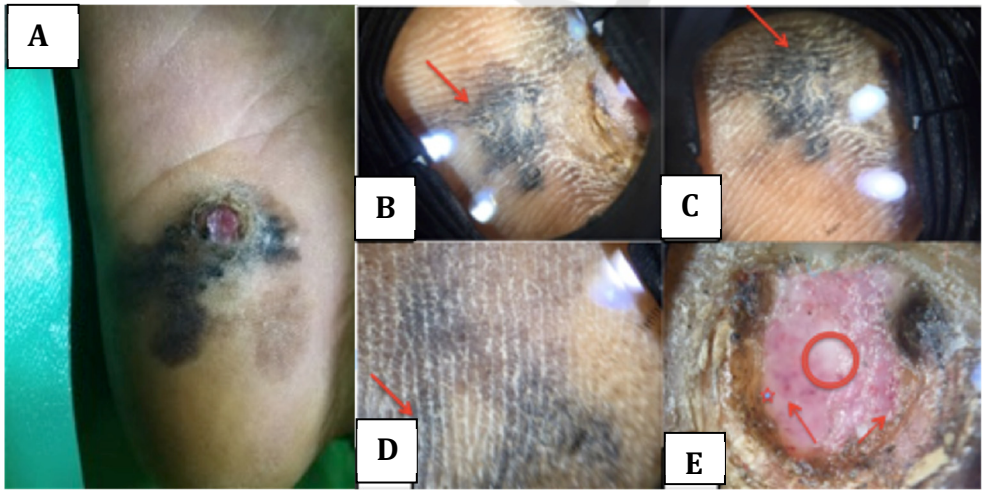

Figure 1: (A) Hyperpigmented lesion on right sole with solitary ulcer on it. Dermoscopic pattern of the lesion (B,C,D,E).

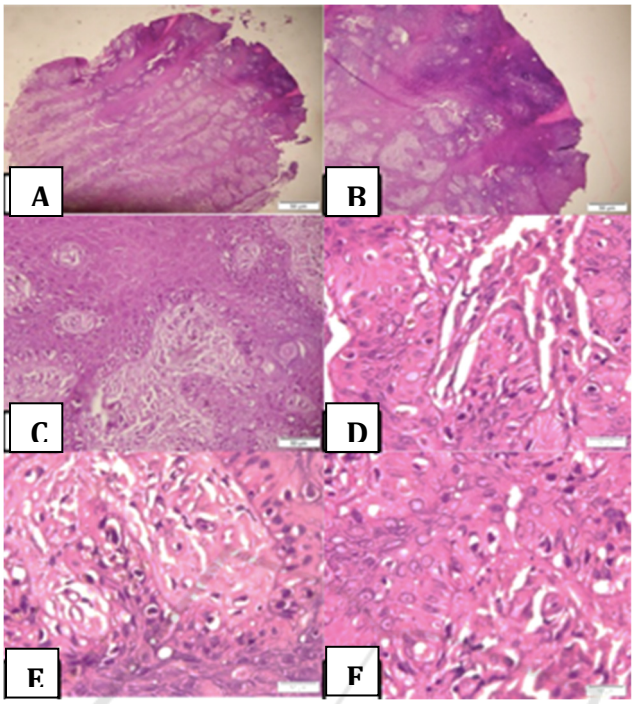

Figure 2: Histopathological image from the lesion suit with acral lentiginous melanoma.

3 DISCUSSION

Melanoma is a tumor derived from melanocytes and can be foundon skin, mucosal, eyes and brain meningeal. Acral melanoma itself is a subtype most commonly found in non-white populations. This subtype includes>70% melanoma in African races in America as well as 50% in Asian racial groups (Ishihara et al., 2008).

Risk factors from melanoma can be divided into 3 categories including genetic factors, phenotypic manifestations of genetic and environmental interactions also environmental factors. Genetic mutations or polymorphism can increase one person's tendency for the development of melanoma. The focus of genes associated with familial melanoma is CDKN2A, which plays a role in coding proteins p16 and p14 that function in the course of cell cycle. In addition, variants of the melanocortin-1 receptor gene (MC1R) were also found to increase the risk of melanoma formation. Factors that are phenotypic manifestations of genetic and environmental interactions are melanocytic nevus, atypical melanocytic nevus and ephelids and lentigo solaris. Environmental factors that play a role in the formation of cutaneous melanoma are ultraviolet radiation; especially ultraviolet B. Chronic radiation can cause mutations and DNA damage which disrupt the cell cycle. In a study that assessed the role of trauma in the occurrence of ALM in areas not exposed to sunlight such as soles of the feet, hands and nails found about 13-55% of cases of ALM has a history of previous trauma, but its relation to the development of melanoma is still unclear (Phan et al., 2006).

Diagnosis of melanoma requires correlation of clinical features, dermoscopy and histopathology. Clinically lesions of melanoma appear as asymmetrical lesions, having irregular edges, has variety of colors, diameters greater than 5 mm and found growth of nodules or regression components in the lesions. The sensitivity of these clinical features to diagnose melanoma can be as high as 70% if performed by an experienced dermatologist. The most common and typical dermoscopic features for ALM are the presence of parallel-ridge patterns that have a specificity of 99%, sensitivity of 86% and a positive predictive value of 84%. The next most common pattern is the brownish-colored pigment found in ALM in situ and invasive ALM. Another feature that can be found is a serrated pattern consisting of a streak image at the edge of

the tumor. Not infrequently also found ALM with ridge pattern accompanied by diffuse pigmentation area. In the case of an invasive ALM it tends to destroy the furrow and ridges images so that it can be seen only structureless pattern and pigmentation spots. In addition it will show more color and structure such as firm edges, irregular dots and globules, atypical streaks, atypical blotches, blue white veil, regression structure and atypical blood vessels (Malvehy and Puig, 2012).

Histopathological examination remains a gold standard in diagnosing melanoma. In ALM, proliferation of atypical melanocytes in the hyperplastic epidermal basal layer can be seen. Atypical melanocytes are arranged one by one in irregular nests in all layers of the epidermis. In the stratum corneum layer melanocytes and melanin granules are spread evenly. In difficult cases immunohistochemical staining may help diagnosis. Dyes that can detect antigens in melanocytes such as HMB45, tyrosinase, Melan-A / MART-1 and S100 are useful in differentiating melanocyte cells with other cells so as to visualize the extent of primary melanoma as well as to help see the focus of melanoma on lymph node biopsy (Garbe and Bauer, 2012; Merkel and Gerami, 2017). The patient in this case shows the dermoscopic appearance which suggesting to be a melanoma lesion, which later on be confirmed from the histopathological examination.

Management of melanoma can be divided into 3 in primary melanoma (stage 1 and 2), melanoma with regional metastasis (stage 3) and melanoma with distant metastasis (stage 4). In primary melanoma therapy is still with surgical excision with the aim of preventing local recurrence or persistent disease. The last recommended guideline for the management of primary melanoma is for in situ melanoma cases an excision surgery of 0.5 cm from the edge of the tumor should be performed, for melanoma with a depth of ≤ 1 mm requires a 1 cm margin from the edge of the tumor, for melanoma depth of ≥ 2 mm minimum 2 cm margin from the edge of the tumor. For cases in difficult locations such as acral, mucous membranes or face Mohs surgery may be a more appropriate choice. Local recurrence is defined as a recurrence of the lesion within 2 cm of the post-excision site. This results from the spread of primary tumor or intralymphatic spread. In such cases it is necessary to re-execute and check on the regional lymph nodes to see if there are any signs of metastasis or not (Garbe and Bauer, 2012; Garbe et al., 2016). The patient is diagnosed with primary acral lentiginous melanoma and was treated with margin of 1 cm and as deep as subcutaneous tissue, with histopathological examination there are no melanoma cells on the edges of the lesion.

The prognosis for melanoma stage 1 is still quite good with proper and rapid management. The survival rate in stage 1 of 93-97% decreased in stage 2 to 53-82%, in stage 3 it was found that 40-78% and got 9-27% for stage 4. Monitoring of patients with melanoma especially the first 5 years is very important, where 90% of metastases occur at that time period. Regular monitoring aims to identify recurrence or early disease progression, can diagnose early primary melanoma and skin cancer in addition to melanoma, provide psychosocial assistance, provide education to prevent patients and families, provide education for patients and families about a self-examination method for early detection of melanoma, as well as for the administration of adjuvant therapy if necessary. The recommended timeframe according to the guidelines in Europe is 2 to 4 times per year for 5 to 10 years (Garbe and Bauer, 2012; Garbe et al., 2016).

4 CONCLUSION

Reported a case of acral lentiginous melanoma in a man with a clinical picture of a black spot on the sole of the foot since 1 year ago without any complaints. The dermoscopy examination, parallel ridge pattern is seen that gives a suggestion of a melanoma lesion. The patient then performed a biopsy and presented atypical melanocytes with bizzare nuclei and also found mitosis so that the diagnosis tends to lead to acral lentiginous melanoma. Patients were consulted to the surgical department for further treatment and performed excision surgery with 1 cm margin. The prognosis of the patients is still need to be established by deciding in the tumor stage, however periodic monitoring is necessary to prevent and diagnose both primary and metastatic melanoma lesions in order to improve survival rates, especially the first 5 years.

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