Melanoma Misdiagnosed as Multiple Diabetic Foot Ulcer: A Case Report

Nadezhda V. Maksimova^{1,2}, Aleksey O. Kovylov³, Mikhail E. Krasheninnikov⁴, Marina V. Kovina⁴, Alexey V. Lyundup^{4,5}, Denis S. Baranovskii^{4,6}, Ilya D. Klabukov^{4,6,7}

Department of Endocrinology, Pirogov Russian National Research Medical University, Moscow, Russia
 Central Clinical Hospital of the Administrative Directorate of the President of the Russian Federation, Moscow, Russia
 State Moscow Endocrine Dispensary, Moscow, Russia

⁴ Research and Educational Resource Center for Cellular Technologies, Peoples' Friendship University of Russia (RUDN University), Moscow, Russia

⁵ N.P. Bochkov Research Center for Medical Genetics, Moscow, Russia

⁶ Department of Regenerative Medicine, National Medical Research Radiological Center, Obninsk, Russia
⁷ Obninsk Institute for Nuclear Power Engineering, National Research Nuclear University MEPhI, Obninsk, Russia

Received: 27 Apr. 2022; Accepted: 21 Nov. 2022

Abstract- Malignant skin ulcerations may mimic diabetic foot ulcers leading to misdiagnosis. In this case report, we discuss an uncommon but severe problem of malignant tumors initially misdiagnosed as diabetic foot ulcers, underlying the need to improve medical awareness, diagnostics, and approaches for therapy once the correct diagnosis is made. We describe the case of an 82-year-old male with diabetes mellitus and melanoma metastases initially misdiagnosed as diabetic foot ulcers. In diabetic patients, several skin disorders may coexist on the same foot, including actual diabetic foot ulcers and skin cancers. Among multiple skin disorders that coexist on the foot of a diabetic patient, the skin metastases may be misdiagnosed as diabetic foot ulcers. Significant efforts should be made to create new non-invasive, rapid diagnostic techniques to eliminate misdiagnoses of skin disorders in diabetic patients.

© 2022 Tehran University of Medical Sciences. All rights reserved. *Acta Med Iran* 2022;60(12):782-784.

Keywords: Diabetic foot ulcer; Melanoma; Misdiagnosis; Skin cancer; Case report

Introduction

Diabetes mellitus (D.M.) is a widespread disease, with each fifth patient over 65 years old (1). Numerous studies have confirmed the influence of diabetes and the patient's age on the risk of melanoma development (2). Skin malignant neoplasms may not have typical cancer features and mimic chronic non-healing wounds. The risk of misdiagnoses rises significantly if a diabetic foot ulcer (DFU) transforms into a malignant tumor. The occurrence of DFU in patients with D.M. (6.3%) (3), the frequency of long-term non-healing ulcers among DFU patients (20%) (4), and the risk of developing malignant skin neoplasms in the population of diabetic patients with non-healing ulcers rise the malignancy alert (5,6). In addition, applying growth factors and cell therapy for DFU treatment make especially important the differential

diagnostics between benign and malignant ulcers.

We described a clinical case of histologically confirmed spindle-shaped cells nodular melanoma in an ulcer originally classified as DFU. We consider this case as a striking call to drive the attention of the medical community to the prevention of repeated facts of an incorrect DFU diagnosis and the following inadequate pro-cancerous treatment, seriously aggravating the disease outcome.

Case Report

An 82-year-old man with a three-year history of D.M. type 2 was admitted to the endocrinology clinic of Sechenov University in April 2018. The patient had a non-healing ulcer on his right heel. Six months before admission, the patient received podiatric care for a

Corresponding Author: I.D. Klabukov

Department of Regenerative Medicine, National Medical Research Radiological Center, Obninsk, Russia Tel: +7 484 3993130, Fax: +7 484 3993130, E-mail address: ilya.klabukov@gmail.com

Copyright © 2022 Tehran University of Medical Sciences. Published by Tehran University of Medical Sciences
This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International license (https://creativecommons.org/licenses/by-nc/4.0/). Non-commercial uses of the work are permitted, provided the original work is properly cited

diabetic ulcer at his community hospital.

On admission, the patient had a 5x5-cm-sized nonpigmented ulcer with a callus-like periphery and a foul smell on the plantar aspect of the right heel. The wound base was covered with fibrin and overgrown granulation tissue that extended beyond the wound edges, and a substantial amount of serous exudate was observed. However, there was no swelling, pain, or hyperemia at the ulcer site. The X-ray of the right foot did not show any evidence of osteomyelitis. Wound sampling revealed the presence of Corynebacterium striatum, Pseudomonas aeruginosa, and methicillin-resistant Staphylococcus aureus in a titer greater than 1x108 CFU/ml. A blood sampling showed an erythrocyte count of 4.31×10¹²/L (reference range (R.R.) from 4 to 6×10¹²/L), leucocytes count of 5.30×10^9 /L (R.R. from 4 to 9×10^9 /L) (neutrophils count of 59.50% (RR from 47 to 72%), 7.00% monocytes (R.R. from 3 to 11%), and 31.60% lymphocytes (R.R. from 19 to 37%)), platelet count of $250\times10^{9}/L$ (R.R. from 180 to $320\times10^{9}/L$) and glycosylated hemoglobin level 6% (R.R. <7%) (the reference ranges are given in brackets) (7). The patient had good pedal pulses. The skin temperature, vibrational pain, and tactile sensitivity decreased in both feet. So, we suggested the presence of peripheral neuropathy. In the Endocrinology clinic of Sechenov University, the wound was initially classified as neuropathic DFU stage 2B (University of Texas classification) and was treated at first with infusions of vancomycin for ten days, and then the antibiotic was changed to ceftazidime infused for 10+ days. Debridement was performed only on the wound edges.

The wound did not show any healing after 20 days of the therapy, suggesting that the initial diagnosis of DFU may not have been warranted. The patient was referred to an oncology unit for a biopsy, where wide excision of the heel ulcer and skin grafting was performed. Histopathological examination showed epithelial spindle cells without involvement of the wound edges, suggesting the diagnosis of malignant nodular spindle-cell melanoma, Clark's level of invasion-3, Breslow thickness-14 mm, Mitotic index-11/mm². The patient refused chemotherapy.

In November 2018, this patient was admitted to the community hospital with a 2x1-cm oval-shaped nonpigmented ulcer with a callus-like periphery on the plantar aspect of the right heel, which reappeared at the site of the previously treated ulcer (Figure 1A). Except for the size, wound characteristics did not differ from what was noticed at the first admission to the endocrinology clinic of Sechenov University, including overgrown granulation and fibrin at the wound base, the substantial amount of serous exudate, no swelling, pain, or hyperemia at the ulcer site. However, two small roundshaped, partly ulcerated masses with eschars on the surface were presented on the lateral side of the right foot (Figure 1B), which were diagnosed as melanoma metastases by an oncologist. From the anamnesis, it was known that a specific treatment was not carried out after the detection of melanoma. The patient has referred again to the oncology unit for further melanoma treatment, and the diagnosis of metastases was pathomorphological confirmed after radical surgical excision of both masses.

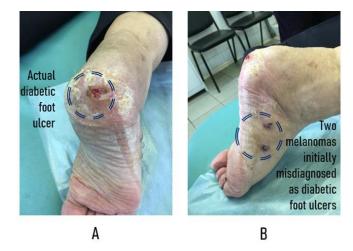


Figure 1. A: The plantar aspect of the patient's right heel with a 2x1-cm sized non-pigmented ulcer with a callus-like periphery. B: The lateral side of the right foot. Two small round-shaped partly ulcerated masses with eschars on the surface were diagnosed as melanoma metastases by a specialist in oncology

Discussion

Despite recent medical progress and modern practical diagnostic tools such as dermoscopy and biopsy, diagnosing sinister tumors in diabetic patients is still challenging. There are no non-invasive medical devices and assays that allow dermatologists to differentiate malignancies from non-neoplastic foot ulcers.

The clinical case of the 82-year-old adult presented here illustrates how nodular spindle melanoma was initially diagnosed as a diabetic ulcer. The suspicion of malignancy was low at admission because the DFU-like lesion did not show any atypical features. The patient's blood count and biochemical assays were also within the normal range. Perhaps, the normal level of glycosylated hemoglobin could raise awareness regarding the nature of the ulcer (cancerous versus diabetic), but this suggestion needs to be further verified.

The initial misdiagnosis caused a 20-day delay in the correct diagnosis of melanoma. The delay in diagnosis might be life-threatening, especially if growthstimulating or metastasis-provoking treatment (stem cells, growth factors, debridement) is applied.

This case is also a good example of a strong similarity between melanoma and diabetic ulcer. It is possible that the malignant etiology of a wound may not be identified at first, also because the clinicians who care for diabetic patients are generally not dermatologists or oncologists. Therefore, it is essential to carry out specific educational efforts and promote consultations with multidisciplinary teams. Another action may be applied to develop noninvasive multispectral screening devices to detect malignant features on skin surfaces. Relevant epidemiological studies are needed to establish the actual number of malignancies initially misdiagnosed as DFUs.

In diabetic patients, several skin disorders may coexist

on the same foot, including actual diabetic foot ulcers and skin cancers. Among the multiple skin disorders that coexist in the foot of a diabetic patient, the skin metastases may be misdiagnosed as diabetic foot ulcers. Significant efforts should be made to create new noninvasive, and rapid diagnostic techniques to eliminate the misdiagnosis of skin disorders in diabetic patients.

References

- International Diabetes Federation (IDF). Diabetes Atlas. Ninth ed, 2019. (Accessed URL: http://www.diabetesatlas.org.)
- Tseng HW, Shiue YL, Tsai KW, Huang WC, Tang PL, Lam HC. Risk of skin cancer in patients with diabetes mellitus: a nationwide retrospective cohort study in Taiwan. Medicine (Baltimore) 2016;95:e4070.
- Zhang P, Lu J, Jing Y, Tang S, Zhu, D, Bi Y. Global epidemiology of diabetic foot ulceration: a systematic review and meta-analysis. Ann Med 2017;49:106-16.
- Dutra LM, Melo MC, Moura MC, Leme LA, De Carvalho MR, Mascarenhas AN, et al. Prognosis of the outcome of severe diabetic foot ulcers with multidisciplinary care. J Multidiscip Healthc 2019;12:349-59.
- 5. Lyundup AV, Balyasin MV, Maksimova NV, Kovina, MV, Krasheninnikov ME, Dyuzheva TG, et al. misdiagnosis of diabetic foot ulcer in patients with undiagnosed skin malignancies. Int Wound J 2022;19:871-7.
- 6. Toussaint F, Erdmann M, Berking C, Erfurt-Berge C. Malignant Tumours Presenting as Chronic Leg or Foot Ulcers. J Clin Med 2021;10:2251.
- Chamberlain JJ, Rhinehart AS, Shaefer CF, Neuman A. Diagnosis and management of diabetes: synopsis of the 2016 American Diabetes Association Standards of Medical Care in Diabetes. Ann Intern Med 2016;164:542-52.