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Case report

Chemotherapy-Induced Asymmetrical Melanonychia

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SUMMARY

Introduction: Chemotherapy may cause various nail damages, including chromonychia, melanonychia, onycholisis, and onychomadesis. Melanonychia is characterized by melanin–derived brown–to–black nail pigmentation. It may occur as a result of nail matrix melanocytic activation or melanocytic hyperplasia, and nail invasion by melanin–producing pathogens.
Case report: We present a case of a patient who developed an extremely rare event of asymmetric melanonychia during systemic treatment of non–Hodgkin lymphoma. The melanonychia developed in dose–dependent manner after 500 mg of doxorubicin. One of the most incriminating agents for melanonychia development are doxorubicin and to a less extent cyclophosphamide. Our patient received both drugs as combined chemotherapy. After treatment completion, the phenomenon disappeared. An extremely unexpected event was skin melanoma occurrence.
Conclusion: It has not been clarified yet whether this event was causally related to previous nail-related melanocyte activation or it was just a coincidence.

Keywords: **chemotherapy, melanonychia, chromonychia**

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INTRODUCTION

Multidrug chemotherapy may express a variable propensity towards morphological nail damaging including chromonychia, melanonychia, onycholysis, and onychomadesis. Melanonychia is characterized by melanin–derived brown–to–black nail pigmentation. It may occur as a result of nail matrix melanocytic activation or melanocytic hyperplasia, and nail invasion by melanin–producing pathogens (1, 2). Regarding etiological factors, melanonychia may be caused by numerous agents: traumatic injuries, fungal infection (3), inflammations or drugs. Among all the aforementioned, particular emphasis should be placed on melanonychia as a chemotherapy-induced phenomenon. Chemotherapy-induced melanonychia usually implies fingernails involvement either of the arms or legs, with a diffuse melanocytic growth pattern. There are almost no data regarding asymmetric melanonychia involvement during multidrug chemotherapy exposure. This case presents a very unusual finding.

CASE REPORT

A 65–year–old male with an advanced stage of non-Hodgkin lymphoma type of Mantle cell lymphoma (MCL) underwent induction chemotherapy treatment with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) regimen for 8 consecutive cycles. The dark bluish coloration of nails slightly developed after 500 mg of cumulative dose of doxorubicin (fifth cycle of chemotherapy). It was clinically presented as melanonychia with a diffuse pattern of distribution resembling subungual hemorrhage (SH). However, it covered in total only 2 left foot nails, while toe fingernail was partially covered. Right leg and hand's nails were spared (Figure 1 A, B, C, D). The dark bluish diffuse coloration did not spread to skin or tongue by the end of treatment. The major differential diagnostic problems were SH, fungal melanonychia (FM) and subungual melanoma (SM). No traumatic injuries were reported by the patient and dark colored nails were painless.

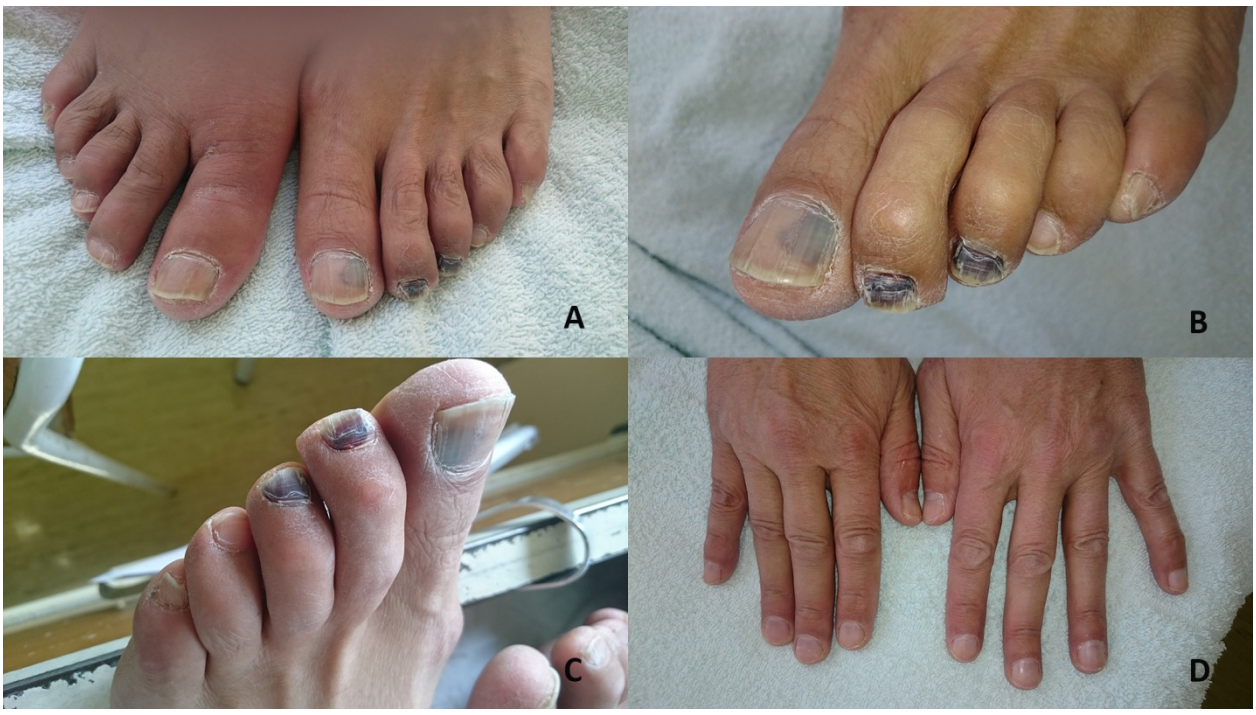

Figure 1. *A, B, C, D. A–A comparison of two feet, highlighting the left finger nails with dark bluish chromonychia. B–A close up view of partially developed dark bluish chromonychia of the left foot, emphasizing total coverage of two nails and partial discoloration of toe finger nail. C–A close up view from other perspective. D–Hand's nails are spared of dark bluish discoloration.*

FM was excluded by dermoscopy-onichoscopy analysis and short duration of the changes. SM was less suspicious since this melanocytic subungual pigmentation appeared suddenly in three different nails; clinical presentation was not a typical (absence of longitudinal pattern with Hutchingson's sign) or progressive growth. The dermoscopic-onychoscopic examination was performed confirming melanocytic proliferation without malignant characteristics. Melanonychia started to resolve within a few months after chemotherapy cessation.

As to lymphoma treatment, the patient was driven to complete remission and underwent regular follow–up visits every 3 months. However, he developed skin melanoma 1.5 years during a follow–up period for MCL located on his back. Melanoma presented in advanced Breslow stage 4. It was skin melanoma without exulceration sign (pT4aN0M0). No distant spreading was found by sentinel node biopsy and by imaging (CT scan of thorax, abdomen and pelvis). Therefore, no specific oncologic treatment was conducted. The patient continued with regular follow–ups for MCL and skin melanoma. Unexpectedly, the patient developed acute coronary event few months after melanoma surgery and died as an emergency case of a heart attack.

DISCUSSION

Chemotherapy exposure may be associated with cutaneous, nail or mucosal coloration as a side effect. In a comprehensive study of 205 patients, it was reported that almost 60% of them developed some kind of nail changes with over 81% presented as diffuse hyperpigmentation of nails (4). Chromonychia, primarily melanonychia, was described after the use of various antineoplastic drugs: doxorubicin, cyclophosphamide, daunorubicin, busulfan, vincristine, bleomycin, 5–fluorouracile, docetaxel, dacarbazine, methotrexate, imatinib, melphalan hydrochloride, etoposide, tegafur (5-10). Nevertheless, most of the reported cases highlight doxorubicin and less frequently cyclophosphamide as agents with high propensity towards melanonychia development (10, 11). Interestingly, our patient developed asymmetric melanotic pigmentation covering only 3 leg nails after receiving 500 mg of doxorubicin. It can be highlighted that melanonychia occurred in dose–dependent manner, having the unique clinical aspect reported so far. It can be assumed that the time interval between the start of therapy and first signs of nail pigmentation might be dependent on the rate of nail growth. This would explain the later and less frequent appearance of changes in the toenails (12). Based on our single center experience, we detected a median of 5 – 10 cases per year of dark bluish chromonychia and melanonychia in patients receiving doxorubicin containing regimens (sole or combined with other antineoplastic drugs, especially with cyclophosphamide). However, all of the cases we registered had symmetrical hand's nails coverage.

Melanocytic activation is the leading cause of chemotherapy-induced melanonychia. Regarding the rarity of the phenomenon and lack of systemic data, a few underlying etiologic factors have been assumed: matrix melanocyte activation (10), endogenous pigments overproduction or storage (10), doxorubicin induced melanocyte–stimulating hormone (MSH) secretion (5), increased melanin pigmentation of the nail matrix epithelium and nail plate without a concurrent increase in the number of melanocytes (13). Some data confirmed doxorubicin–induced increased melanin deposition in epidermis, particularly in the basal layer (6). Patients receiving anthracyclins (doxorubicin) that contain regimens are at risk of melanonychia development. It has not been clarified why only a small portion of patients develop melanocytic activation. A merely unique clinical aspect presented in this case may be a differential problem with SH, FM, and rarely SM. However, onychoscopy analysis has the discriminating power in determination of differential diagnosis. Nail discoloration resolves within weeks or months after chemotherapy cessation, and it is rather a cosmetic problem, not clinically significant.

However, it is evident that presented patient developed skin melanoma during a period of follow–up. It has been undetermined yet whether this event was causally related to previous nail-related melanocyte activation or it was just a coincidence.

Conflict of interest

I declare NO conflict of interest

References

1. Jefferson J, Rich P. Melanonychia. Dermatol Res Prac 2012;2012:952186. https://doi.org/10.1155/2012/952186

2. Sobjanek M, Wlodarkiewicz A, Tobola J. Melanonychia longitudinalis. Adv Dermatol Allergol 2006; 23(3):130-137.

3. Elmas ÖF, Metin MS. Dermoscopic findings of fungal melanonychia. Adv Dermatol Allergol 2020;37(2):180-183. https://doi.org/10.5114/ada.2020.94836

4. Saraswat N, Sood A, Verma R et al. Nail changes induced by chemotherapy agents. Indian J Derm 2020;65(3):193-498. https://doi.org/10.4103/ijd.IJD_37_19

5. Casamiquela KM, Cohen PR. Chemotherapy-associated tongue hyperpigmentation and blue lunula. J Drugs Dermatol 2013;12(2):223-226.

6. Abbasi NR, Wang N. Doxorubicin-induced hyperpigmentation. Dermatol Online J 2008;14(10):18. https://doi.org/10.5070/D365M8X79P

7. Gilbar P, Hain A, Peereboom VM. Nail toxicity induced by cancer chemotherapy. J Oncol Pharm Pract 2009;15(3):143-155. https://doi.org/10.1177/1078155208100450

8. Prajapati VB, Madhyastha S, Acharya R et al. Cyclophosphamide and Doxorubicin Induced Melanonychia: A Case Report. J Clin Diagn Res 2017;11(1):OD04-OD05.

9. Mendiratta V, Jain A. Nail dyschromias. Indian J Dermatol Venereol Leprol 2011;77(6):652-658. https://doi.org/10.4103/0378-6323.86473

10. Andre J, Lateur N. Pigmented nail disorders. Dermatol Clin 2006;24(3):329-339. https://doi.org/10.1016/j.det.2006.03.012

11. Mehta S, Makkar V, Soha PM et al. Cyclophosphamide-induced melanonychia in a patient with steroid dependent nephrotic syndrome: A rare presentation. Saudi J Kidney Dis Transpl 2019;30(4):978-981. https://doi.org/10.4103/1319-2442.265478

12. M I, Khairkar PH. Doxorubicin induced melanonychia. Indian Pediatr 2003;40(11):1094-1095.

13. Ghupta A, Parakh A, Dubey PA. Chemotherapy induced nail changes. Ind J Derm 2008;53(4):204-205. https://doi.org/10.4103/0019-5154.44804

Asimetrična melanonihija prouzrokovana hemioterapijom

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SAŽETAK

Uvod. Hemioterapija može izazvati raznovrsne tipove oštećenja noktiju, kao što su hromonihija, melanonihija, oniholiza ili onihomadeza. Melanonihija predstavlja melaninsku pigmentaciju nokta od braon do crne boje. Ona se može pojaviti kao rezultat aktivacije melanocita nokatnog matriksa ili hiperplazije melanocita i može nastati invazijom nokatne ploče od strane patogena koji produkuju melanin.
Prikaz bolesnika. Prikazujemo slučaj bolesnika koji je razvio ekstremno retku pojavu asimetrične melanonihije tokom sistemske terapije nehočkinovog limfoma. Melanonihija se razvila shodno dozi, nakon primene 500 mg doksorubicina. Jedan od najznačajnijih agenasa za razvoj melanonihije je doksorubicin i, u manjoj meri, ciklofosfamid. Naš bolesnik primio je oba leka kao kombinovanu hemioterapiju. Po završetku tretmana fenomen je nestao. Izuzetno neočekivani događaj bio je pojava melanoma kože.
Zaključak. Da li je ovaj događaj uzročno povezan sa prethodnom aktivacijom melanocita nokatne ploče ili je to bila samo slučajnost, ostaje nepoznanica.

Ključne reči: **hemioterapija, melanonihija, hromonihija**