Acta Dermatovenerol APA

Acta Dermatovenerologica
Alpina, Pannonica et Adriatica

2025;34:89-93
doi: 10.15570/actaapa.2025.18

Two cases of bizarre acquired localised hyperpigmentation disorders – similar yet different diagnostic challenges: two case reports and a brief literature review

Laura Đorđević Betetto[1]✉, Boštjan Luzar[2,3], Aleksandra Bergant Suhodolčan[1,3]

[1]Department of Dermatovenerology, Ljubljana University Medical Center, Ljubljana, Slovenia. [2]Institute of Pathology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia. [3]Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia.

Abstract

Cutaneous pigmentation disorders are one of the leading causes of dermatological consultation globally. Hyperpigmentation disorders constitute a group of distinct medical conditions that may be either congenital and associated with various concurrent comorbidities, or acquired due to cutaneous, environmental, or systemic conditions or factors. Due to numerous causes and an often atypical clinical picture, diagnosis can be challenging. Furthermore, although the changes in skin color are not inherently harmful, they can result in significant cosmetic disfigurement and have psychological and social repercussions, particularly given that some hyperpigmentation is irreversible due to the limited effectiveness of current treatments. This article presents two cases exhibiting somewhat similar but different acquired localized hyperpigmentation. We review the current literature with emphasis on the diagnostic approach to this entity and specific acquired hyperpigmentation disorders, in particular drug-induced and paraneoplastic. We emphasize the importance of interdisciplinary cooperation among different specialists, particularly in complicated cases and those that accompany systemic diseases.

Keywords: acquired hyperpigmentation, drug-induced hyperpigmentation, minocycline, POEMS syndrome, monoclonal plasma cell disorder

Received: 6 November 2024 | **Returned for modification:** 13 March 2025 | **Accepted:** 15 March 2025

Introduction

Hyperpigmentation is darkening of the natural skin color, typically due to increased melanin deposition and occasionally to the deposition of endogenous or exogenous pigments such as hemosiderin or heavy metals (1). It is a feature of many clinical conditions, not only inherited and acquired syndromes, but also physiological variations in skin color, particularly in individuals with darker skin phototypes (1–3). Although benign, hyperpigmentation may indicate a serious condition and should therefore not be regarded simply as a cosmetic concern.

This article examines acquired localized hyperpigmentation and its evaluation using two similar cases. The patients are both middle-aged men with similar comorbidities, most notably an underlying monoclonal plasma cell disorder. Both presented with a unique dark hyperpigmentation that required extensive diagnostic workup and multiple skin biopsies.

Case reports

Patient one

A 73-year-old man presented to our clinic in June 2023 with a hyperpigmented skin lesion on his upper right thigh. The patient first noticed the discolored skin during autumn 2021. He had severe pain in his right hip and developed a fever during the summer of the same year. He was diagnosed with *Staphylococcus aureus* sepsis that stemmed from either cellulitis with an abscess or pyogenic myositis in the hip region. He was treated with flucloxacillin for 10 days before being discharged from hospital. When he returned home, a red discoloration on his right thigh below the hip joint developed together with increasing pain followed by edema, and finally a grayish-black discoloration of the skin appeared. Following suspicion of an infection in a right hip prosthesis inserted over 5 years earlier, further diagnostics ruled out joint pathology. In May 2022, an orthopedic surgeon prescribed oral minocycline at a dosage of 100 mg twice daily for a protective treatment that was to last several months. The treatment eliminated the redness and relieved the pain. However, the black color persisted and worsened. The patient denied the development of skin changes after sun exposure or application of ointments. A skin biopsy in November 2022 revealed mild perivascular and periadnexal mononuclear cell dermatitis with reticular dermal collagen formation. The histological changes were non-specific. An infectious diseases specialist recommended eventual discontinuation of treatment with minocycline because there were no signs of infection. In March 2023, a soft tissue ultrasound indicated subcutaneous fat irritation and increased blood flow.

The patient had a history of hypertension and benign prostatic hyperplasia. He has regular hematological checkups for smoldering immunoglobulin (Ig) A kappa multiple myeloma. His hematologic disease has remained stable, and he has not received any specific therapy since February 2022. The last follow-up examination in April 2023 showed no clinical or laboratory signs of disease progression. He had undergone bilateral hip arthroplasty. He was taking tamsulosin, telmisartan, carvedilol, acetylsalicylic acid, and minocycline. He has no family history of dermatological disorders.

During the clinical examination at our clinic, an area of uneven black discoloration was present on the lateral part of the right thigh, consisting of several confluent, mostly round, non-scaly macules. The skin structure itself was not altered, there was no atrophy or

✉ Corresponding author: laura.betetto@gmail.com

sclerosis, and the skin appendages were preserved. The black discoloration was irregularly spreading into the surrounding skin, where the pigmentation decreased (Fig. 1). A similar, albeit smaller, lesion was located on the anterior aspect of the thigh at approximately the same level. Non-melanin deposition of grayish and brownish perifollicular pigment was visible on dermoscopy. Notably, the skin did not show hyperpigmentation in the area of the hip replacement scar or elsewhere on the body or mucous membranes.

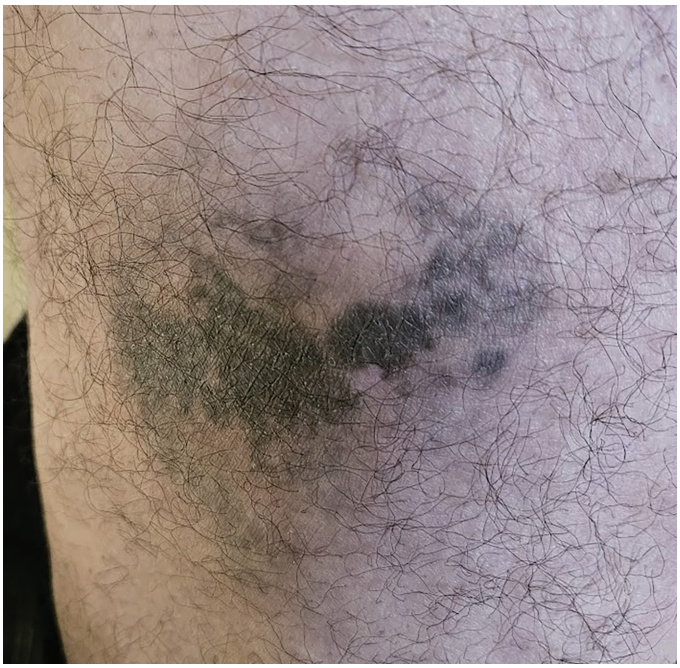

Figure 1 | Patient 1 at the time of presentation: hyperpigmentation on the upper thigh.

Upon reexamination of the first skin biopsy, pigment was found deposited within macrophages and freely in the interstitium both in the dermis and in certain regions of the subcutaneous fat and along the skin adnexa. The pigment stained positive to histochemical staining with Perls Prussian blue and Fontana–Masson stain (FM) with an accompanying mild, predominantly chronic perivascular and partially interstitial lymphocytic infiltrate. The histologic changes observed were consistent with minocycline pigmentation (Fig. 2). Positive histochemical reactions to Perls and FM indicated the presence of a minocycline derivative and suggested type 2 minocycline pigmentation (Fig. 3 A, B).

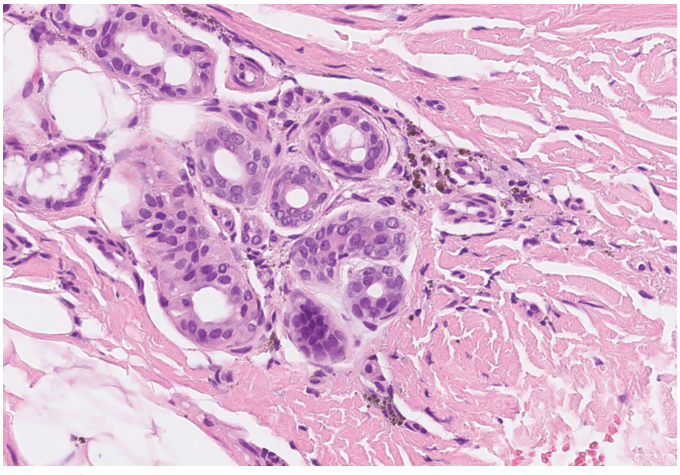

Figure 2 | Histopathological findings: dark pigment granules deposited in the dermis and subcutis, and along the skin adnexa.

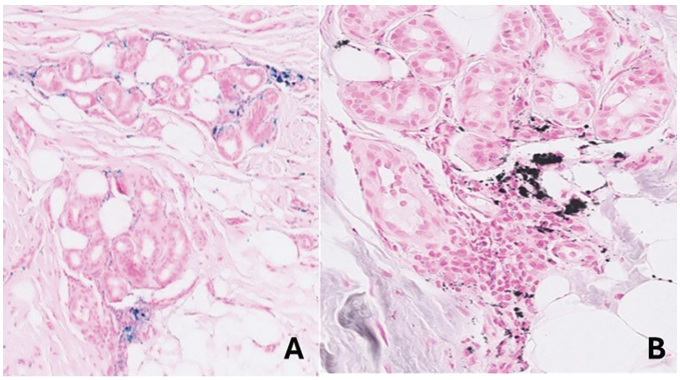

Figure 3 | Positive histochemical reactions to (A) Perls and (B) Fontana–Masson indicative of type 2 minocycline-induced hyperpigmentation.

We advised strict sun protection and recommended discontinuation of minocycline therapy. After the orthopedic examination, the patient stopped taking minocycline at the end of August 2023, having taken it for a total of 14 months. During his October 2023 dermatological check-up, the patient reported no change in pigmentation on the right thigh and no new lesions. However, on clinical examination, an improvement was noted: the pigmentation was less pronounced and receding compared to the previous examination. Because the patient did not express any concerns about the cosmetic appearance of the lesion and was told that it would gradually fade, no further treatment was initiated.

Patient two

A 74-year-old male patient first presented to our clinic in March 2023 with a hyperpigmented patch on the tip of his nose, which he had noticed since the beginning of 2021. Initially, the lesion caused mild itching, but it then became asymptomatic and remained stable without darkening, spreading, or changing in any other way. The patient denied any association with nose inflammation or injury, and he was uncertain of its exact onset.

The patient has a medical history of benign prostatic hyperplasia, type II diabetes, hyperlipidemia, arterial hypertension, chronic obstructive pulmonary disease (COPD), and right fibrothorax. He was taking metformin, tamsulosin, rosuvastatin, a combination of enalapril and hydrochlorothiazide, a combination of fenoterol and ipratropium inhaler, and a combination of beclomethasone, formoterol, and glycopyrronium bromide inhaler. His family history is negative for dermatological disorders.

So far, he has been treated by dermatologists at another hospital, where they have carried out two biopsies. The first biopsy showed a slightly denser periadnexal chronic inflammatory cell infiltrate and elastosis in the surrounding dermis. The specimen was sent for review to another pathologist, who described an early actinic keratosis in the background of a solar lentigo. Dilated vessels, some pigment incontinence, a mild perivascular lymphocytic infiltrate, and scattered multinucleated cells were observed in the dermis, with the multinucleated cells possibly being fibroblastic or histiocytic in origin. Although the histologic changes were uncharacteristic, they did not rule out the possibility of rosacea. Topical therapy with mometasone ointment was prescribed once to twice daily for several months, but no improvement was observed.

A second biopsy showed normal nasal skin with only slightly increased solar elastosis and some deposition of light material in the dermis. The patient was referred by an otorhinolaryngologist for several chest X-rays; however, the scans from 2018 showed no

changes in dynamics from 2018, and no malignant changes were detected. He was then referred to our clinic for further treatment.

On our initial clinical examination, a single, sharply demarcated, irregular, bluish-gray macule was observed on the tip of the nose, with no papules or scales present (Fig. 4A). No similar changes were noted on other areas of the skin or mucous membranes. The patient's skin showed signs of chronic actinic damage. No characteristic features or vessels were noted dermoscopically, only diffuse bluish-gray dermal pigment deposits and two shallow scars from previous biopsies (Fig. 4B). In March 2023, a consensus expert panel of dermatologists from our clinic concluded that the skin changes could not be etiologically defined at that time. The recommendation was to review the second biopsy and take a thorough medical history focusing on possible triggers of the pigmentation.

A comprehensive medical history, including the use of various drugs, ointments, nasal sprays, smoking habits, and exposure to heavy metals, was documented; however, it did not clarify his condition. Regular laboratory tests conducted every 6 months and an abdominal ultrasound scan revealed no significant abnormalities. The patient attended regular appointments with a pulmonary specialist for poorly controlled COPD, presenting with exertional dyspnea and generalized weakness. The patient reported no alarming complaints other than an unintentional weight loss of about 10 kg over the past year.

A revision of the second biopsy showed actinic keratosis with superficial scarring resulting from the previous biopsy. Solar elastosis was also present, and some hemosiderin pigment deposition was found in the dermis beneath the scar. The deposition was attributed to a previous procedure. The staining tests for amyloid and fungi were negative, but the hemosiderin pigment in the dermis was Perls positive.

At the dermatological follow-up in April 2023, no change in nasal hyperpigmentation was observed. Because the biopsy revealed actinic keratosis, a standard treatment plan involving topical 5% imiquimod cream was prescribed.

As a result of the weight loss, the diabetologist discontinued the metformin therapy. The examination of complete blood count, C-reactive protein, erythrocyte sedimentation rate, serum protein electrophoresis (SPEP) with immunofixation, serum free light chain (FLC) assay, Ig levels, and urine protein electrophoresis (UPEP) with immunofixation revealed mild macrocytic macrochromic anemia. Significant was the detection of a monoclonal IgA kappa protein in the serum at a concentration of 4.0 g/l, an increase in the free light chain kappa (358.0), and an abnormal (increased) free light chain ratio (23.71). There were also corresponding findings of monoclonal IgA kappa protein and elevated free light chain kappa in the urine. Due to the suspicion of monoclonal gammopathy of undetermined significance (MGUS), the patient was referred to a hematologist for further diagnostic clarification. A bone marrow aspiration and biopsy revealed bone marrow infiltration of about 5% with monoclonal plasma cells expressing the kappa and lambda light chains in a ratio of about 5:1, consistent with MGUS. There were also reactive changes in orthotopic hematopoiesis. Based on all investigations, the diagnosis of disseminated plasmacytoma could not be made. A diagnosis of MGUS IgA kappa with possible renal involvement was made. At the time of writing of the article, the patient is awaiting nephrology evaluation and presentation at the consensus expert hematology–nephrology MGUS council. Computed tomography (CT) scans with contrast medium of the lungs were ordered to rule out expansive lesions, which showed no remarkable changes compared to the previous scans.

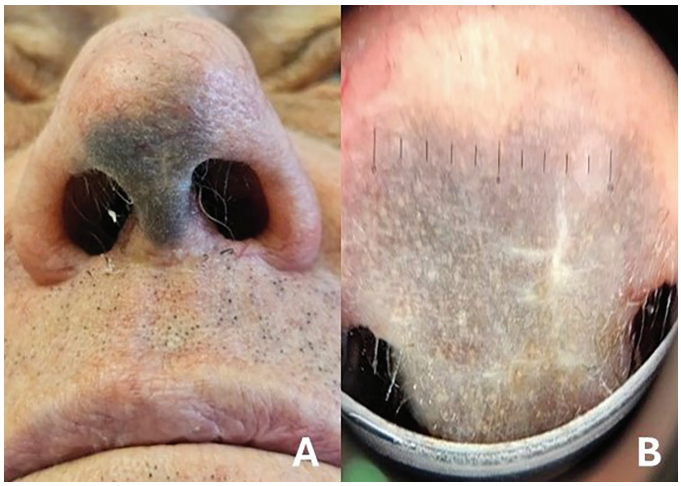

Figure 4 | Patient 2 at the time of presentation: (A) hyperpigmentation on the tip of the nose, (B) dermoscopy showing diffuse bluish-gray dermal pigment deposits and biopsy scars.

At his dermatological check-up in October 2023, the hyperpigmentation on the nose was still unchanged. The patient did not use the prescribed therapy with imiquimod. Since discontinuing metformin therapy, he has regained almost all the weight he had previously lost. His main complaint was exacerbations of COPD over the past year, which required short-term treatment with systemic corticosteroids. His follow-up blood work revealed stable anemia, decreased folic acid and vitamin B12, and abnormal renal function test results (elevated urea and creatinine and decreased estimated glomerular filtration rate). No clinical changes were detected in the hyperpigmentation on the nose and the patient refused treatment because it did not cause any discomfort, and so we decided to discontinue dermatological follow-up and only recommended regular follow-up with other specialists and appropriate sun protection.

The diagnosis of his hyperpigmented lesion on the nose remains a mystery. It is most probably a combination of skin changes caused by chronic sun exposure and a local inflammatory process or injury. The possibility of drug- or tobacco-induced pigmentation is also intriguing, but the lesion lacks characteristic histopathologic changes for this diagnosis (or any other).

Discussion

The diagnosis of acquired hyperpigmentation can be challenging due to a variety of possible causes. The literature suggests an algorithmic approach based on a detailed history and careful physical examination, including extracutaneous sites. Information should be obtained on the onset, duration, progression, localization, definition, pattern, and association of pigmentation with inflammation, injury, systemic disease, medications, smoking, sun exposure, and chemical exposure. A thorough inspection of the skin should be performed to determine the extent, color, shape, distribution (e.g., sun-exposed areas), and pattern of pigmented lesions. Concomitant cutaneous and extracutaneous signs and symptoms should not be overlooked because they can point to the correct diagnosis, especially in cases in which hyperpigmentation is associated with genetic and systemic syndromes (1, 2).

A Wood's lamp is a valuable diagnostic tool to identify the predominant site of pigment deposition in the skin. Epidermal hypermelanosis appears light to dark brown under natural light and

is further emphasized by a Wood's lamp. The contrast between affected and unaffected skin is also increased. In contrast, dermal hypermelanosis appears bluish or gray with less sharply defined borders than epidermal hypermelanosis. In addition, this type of hypermelanosis is not enhanced by a Wood's lamp (4). Dermoscopy is another useful tool to identify and differentiate pigmentary disorders and to assess response to treatment (5). A skin biopsy is another conventional diagnostic method used to evaluate hyperpigmentation disorders, although its use is nowadays limited to atypical clinical presentations or when malignancy is suspected. Standard and special stains such as FM indicate the localization, amount, and type of deposited pigment and melanocytes in the skin (6).

Drugs and chemicals are one of the most common causes of acquired localized and, more frequently, diffuse cutaneous hyperpigmentation. The condition results from increased production of melanin and/or deposition of drug complexes or metals in the skin (1, 7). The list of suspected agents is long, although there is little evidence of a causal relationship for most drugs (8). The diagnosis of drug-induced hyperpigmentation is a dermatologic challenge due to the lack of direct evidence or insufficient information. As more patients, especially the elderly, receive polypharmacy, it is increasingly difficult to associate a pigment change with a specific drug, especially when the chronology between taking the drug and the onset of hyperpigmentation is unknown. A differential diagnosis with hyperpigmentation caused by endocrine and metabolic disorders, the most closely related disorders to drug-induced hyperpigmentation, and with hyperpigmentation of idiopathic origin, should be performed (9). Among the best-known and most common drugs causing hyperpigmentation are chemotherapeutic agents, antimalarials, hormones, heavy metals, prostaglandin agonists, nonsteroidal anti-inflammatory drugs, amiodarone, tetracyclines, zidovudine, psychotropic drugs, tobacco, and psoralens (10).

Our first patient was diagnosed with minocycline-induced hyperpigmentation (MIH). This is a well-documented adverse effect of this tetracycline antibiotic, which is used to treat rosacea, acne, rheumatoid arthritis, and orthopedic infections (11–14). The incidence varies from low in patients with acne vulgaris to high in patients with chronic infections undergoing long-term therapy (12, 15, 16). It has been suggested that higher dosage and long-term therapy together with advanced age may be associated with an increased risk of hyperpigmentation (11, 12, 15–17).

The exact mechanism of MIH remains unknown. Multiple theories have been proposed, including siderosis, melanocyte enhancement, and derivatives of minocycline forming insoluble complexes chelated to iron and calcium (14, 15, 18). MIH may affect several body sites, not only the skin, including the thyroid, bones, teeth, fingernails, toenails, eyes, cartilage, mucus membranes (oral cavity), cardiac valves, and breast milk (11, 15, 19).

Traditionally, three types of MIH have been described, with a fourth one found in a few case reports (17, 20). Type 1, the most common, is characterized by bluish-black macules localized to areas of scarring or previous inflammation. They mainly occur on the face in the context of acne scars, although they have also been reported on other parts of the body; for example, on various sites of inflammation caused by lepromatous leprosy or on the legs after sclerotherapy. On histopathology, the bluish-black pigment stains positive with Perls Prussian blue (iron) and is found in the dermis and scar tissue, extracellularly, and intracellularly in macrophages. It is likely caused by the deposition of pigmented granules, thought to be iron chelates of minocycline (8, 9, 11, 13, 17).

Type 2 appears as bluish-black, brown, or slate-gray pigmentation occurring on healthy skin, predominantly on the lower extremities (shins and ankles). Perls Prussian blue and FM (melanin) colorations are positive in this type. The pigment is found in the dermis and subcutis, outside and within macrophages, and in myoepithelial cells. It is thought to be due to the deposition of pigmented metabolites of minocycline (8, 9, 11, 13, 17).

Type 3, also called dirty skin syndrome, presents as a muddy-brown, generalized, and symmetrical discoloration of healthy skin that is accentuated in sun-exposed areas (11, 21). It resembles a persistent deep-brown tan and is associated with elevated melanin levels. The pigment stains positive for melanin but not for iron and is found in the epidermis, dermis, and macrophages (8, 9, 11, 13, 17, 21).

Finally, type 4 is a bluish-gray pigmentation that occurs in scarred areas on the back. It has the same etiology as type 3 but is localized and not limited to sun-exposed areas. The pigment is positive with von Kossa staining for calcium in addition to melanin staining (FM) (8, 13, 17, 20).

In our case, the MIH obviously developed at the site of a previous inflammation on the right thigh and nowhere else on the body, which is emphasized by the fact that the scar on the left hip/thigh was not affected. This observation and the color of the lesion are characteristic of type 1, but the histopathological changes clearly correspond to type 2. It is therefore plausible that this is a mixed type of MIH because it has features of both type 1 and type 2. Patients with features of several different types of MIH have been described in the literature (11), but to our knowledge not in a single lesion.

Upon diagnosis of MIH, immediate discontinuation of minocycline is recommended to prevent potential pigmentation darkening (11). Patients should also be advised to use photoprotection and cosmetic camouflage, if needed (22). Whereas type 1 and 2 cases usually resolve within months to years after discontinuation of the drug, type 3 pigmentation can be permanent along with pigmentation of other parts of the body (11). Successful treatment with a Q-switched laser has been reported (23). Although MIH is considered a harmless condition, it can lead to permanent cosmetic disfigurement. Therefore, physicians must inform their patients about the possibility of developing MIH during minocycline therapy and monitor them accordingly (11, 12, 18).

In addition, physicians prescribing minocycline need to be aware of this potential adverse effect to avoid confusion and unnecessary testing to rule out other causes of acquired hyperpigmentation (11). This leads to the second patient, who presented an even greater diagnostic challenge and for whom the exact cause of his hyperpigmentation is still unknown. This patient also had an underlying monoclonal plasma cell disease, similar to the first patient. This is likely only a coincidence and not clinically significant.

It should be noted that acquired hyperpigmentation of the skin can be a rare but significant indicator of a hematologic malignancy; specifically, polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder, and skin changes (POEMS) syndrome. POEMS syndrome is a rare multisystem paraneoplastic condition characterized by a monoclonal plasma cell disorder, peripheral neuropathy, and other characteristic features. Skin lesions are one of the minor criteria for the diagnosis of POEMS syndrome and are present in a large majority of patients, most of whom present with multiple dermatologic manifestations (24, 25).

Skin changes linked with the syndrome include hyperpigmentation, hemangiomas and telangiectasia, hypertrichosis, acrocyanosis, white nails, sclerodermoid skin changes, Raynaud's phenomenon, flushing, clubbing, rubor, and hyperemia/erythema. Hyperpigmentation is the most common cutaneous manifestation and is present in almost half of patients. It mainly affects the extremities, but it can also affect other areas of the skin, such as the trunk, nipple complex, head, and neck, or it can be generalized. The hyperpigmentation on the affected areas is diffuse and non-patterned, and it has a dark brown color. Treatment of the underlying hematologic disorder has been associated with improvement of all skin manifestations, including hyperpigmentation (25).

The diagnosis of POEMS syndrome was unlikely in the second patient because peripheral neuropathy, a mandatory diagnostic criterion, was absent. Remarkably, that patient had bone marrow biopsy findings comparable to most POEMS patients. Normally, the median level of plasmacytosis in the bone marrow is less than 5%, and so it can easily be missed on a sporadic bone marrow analysis. Similarly, serum monoclonal protein levels may also be low and undetected if only SPEP without immunofixation, FLC assay, or UPEP is used (26). Although a true malignancy was not confirmed in this case, it serves as a reminder that hyperpigmentation of the skin may conceal a potential malignancy, a diagnostic possibility that must always be considered.

Finally, these cases illustrate the important collaboration between dermatologists and pathologists and the need to provide useful clinical data to obtain an accurate diagnosis.

Conclusions

We presented two different cases of acquired localized hyperpigmentation with an accompanying coincidental monoclonal plasma cell disorder, the first drug-induced and the second unexplained. The aim of this article is to raise awareness of the various etiological factors contributing to localized hyperpigmentation. Although commonly diagnosed, this condition is frequently oversimplified in the era of modern dermatology. It may not only be of cosmetic concern but may also be the first sign of systemic disease, including malignancy.

References

1. Vashi N, Kundu RV. UpToDate. Acquired hyperpigmentation disorders [Internet]. [cited 2023 Nov 4]. Available from: https://www.uptodate.com/contents/acquired-hyperpigmentation-disorders/.
2. Lapeere H, Boone B, De Schepper S, Verhaeghe E, Van Geel M, Ongenae K, et al. Fitzpatrick's dermatology in general medicine. 8th ed. New York: McGraw-Hill; 2012. Chapter 75, Hypomelanoses and hypermelanoses; p. 804–26.
3. Davis SA, Narahari S, Feldman SR, Huang W, Pichardo-Geisinger RO, McMichael AJ. Top dermatologic conditions in patients of color: an analysis of nationally representative data. J Drugs Dermatol. 2012;11:466-73.
4. Gilchrest BA, Fitzpatrick TB, Anderson RR, Parrish JA. Localization of malanin pigmentation in the skin with Wood's lamp. Br J Dermatol. 1977;96:245–8.
5. Krueger L, Saizan A, Stein JA, Elbuluk N. Dermoscopy of acquired pigmentary disorders: a comprehensive review. Int J Dermatol. 2022;61:7–19.
6. Rapini RP. Practical dermatopathology. 2nd ed. Philadelphia: Elsevier Mosby; 2012.
7. Wolff K, Johnson RA, Saavedra AP, Roh EK. Fitzpatrick's color atlas and synopsis of clinical dermatology. 8th ed. New York: McGraw-Hill Education; 2017.
8. Krause W. Drug-induced hyperpigmentation: a systematic review. J Dtsch Dermatol Ges. 2013;11:644–51.
9. Giménez García RM, Carrasco Molina S. Drug-induced hyperpigmentation: review and case series. J Am Board Fam Med. 2019;32:628–38.
10. Kang S, Lerner EA, Sober AJ, Levine N. Pigmentary disorders from exogenous causes. In: Levine N, editor. Pigmentation and pigmentary disorders. Boca Raton (FL): CRC Press; 1993; p. 417–38.
11. Eisen D, Hakim MD. Minocycline-induced pigmentation. Incidence, prevention and management. Drug Saf. 1998;18:431–40.
12. Hanada Y, Berbari EF, Steckelberg JM. Minocycline-induced cutaneous hyperpigmentation in an orthopedic patient population. Open Forum Infect Dis. 2016;3:ofv107.
13. Fiscus V, Hankinson A, Alweis R. Minocycline-induced hyperpigmentation. J Community Hosp Intern Med Perspect. 2014;4:10.3402/jchimp.v4.24063.
14. Geria AN, Tajirian AL, Kihiczak G, Schwartz RA. Minocycline-induced skin pigmentation: an update. Acta Dermatovenerol Croat. 2009;17:123–6.
15. Goulden V, Glass D, Cunliffe WJ. Safety of long-term highdose minocycline in the treatment of acne. Br J Dermatol. 1996;134:693–5.
16. Roberts G, Capell HA. The frequency and distribution of minocycline induced hyperpigmentation in a rheumatoid arthritis population. J Rheumatol. 2006;33:1254–7.
17. Schadler ED, Cibull TL, Mehlis SL. A severe case of minocycline-induced hyperpigmentation of the lower extremities. Cureus. 2018;10:e2672.
18. Rodriguez K, Wellman C, Franks AM, McClelland K, Bannister T. Pigmentary and other dermatologic manifestations of minocycline: a reminder of adverse effects. Marshall J Med. 2019;5:21.
19. Kerbleski GJ, Hampton TT, Cornejo A. Black bone disease of the foot: a case study and review of literature demonstrating a correlation of long-term minocycline therapy and bone hyperpigmentation. J Foot Ankle Surg. 2013;52:239–41.
20. Mouton RW, Jordaan HF, Schneider JW. A new type of minocycline-induced cutaneous hyperpigmentation. Clin Exp Dermatol. 2004;29:8–14.
21. Simons JJ, Morales A. Minocycline and generalized cutaneous pigmentation. J Am Acad Dermatol. 1980;3:244–7.
22. Halder RM, Nordlund JJ. The pigmentary system: physiology and pathophysiology. 2nd ed. Oxford: Blackwell; 2006. Chapter 59, Topical treatment of pigmentary disorders; p. 1163–74.
23. Collins P, Cotterill J. Minocycline-induced pigmentation resolves after treatment with the Q-switched ruby laser. Br J Dermatol. 1996;136:317–9.
24. Dispenzieri A. UpToDate. POEMS syndrome [Internet]. [cited 2023 Nov 4]. Available from: https://www.uptodate.com/contents/poems-syndrome/.
25. Miest RY, Comfere NI, Dispenzieri A, Lohse CM, el-Azhary RA. Cutaneous manifestations in patients with POEMS syndrome. Int J Dermatol. 2013;52:1349–56.
26. Dispenzieri A, Kyle RA, Lacy MQ, Rajkumar SV, Therneau TM, Larson DR, et al. POEMS syndrome: definitions and long-term outcome. Blood. 2003;101:2496–506.