

- 12 Kawaguchi M, Mitsuhashi Y, Kondo S. Iatrogenic hypercalcemia due to vitamin D<sub>3</sub> ointment (1,24 (OH)<sub>2</sub>D<sub>3</sub>) combined with thiazide diuretics in a case of psoriasis. *J Dermatol*, 2003; 30: 801–804.
- 13 Ohigashi S, Tatsuno I, Uchida D, *et al.* Topical treatment with 22-oxacalcitriol (OCT), a new vitamin D analogue, caused severe hypercalcemia with exacerbation of chronic

renal failure in a psoriatic patient with diabetic nephropathy; a case report and analysis of the potential for hypercalcemia. *Intern Med* 2003; 42: 1202–1205.

- 14 Ma Y, Khalifa B, Yee YK, *et al.* Identification and characterization of noncalcemic, tissue-selective, nonsteroidal vitamin D receptor modulators. *J Clin Invest* 2006; 116: 892–904.

### Dermatitis simulata: the mystery of the blue girl

#### Introduction

Secretion of colored sweat by sweat glands is referred to as chromhidrosis.<sup>1</sup> Pseudochromhidrosis refers to the coloration of otherwise colorless sweat on the surface of the skin due to exogenous dyes and paints or chromogenic microorganisms such as *Corynebacterium* or *Piedraia*.<sup>2</sup> We describe here a case of an extensively blue pseudochromhidrosis recently seen in our dermatologic clinic.

#### Case report

A 19-year-old woman consulted our dermatology clinic with intermittent blue staining of her clothes following physical activity. Her mother, a primary care physician, had noticed this affliction 2 months prior the appointment. The sweat was present intermittently after exercising, lasting for some days and vanishing without notice. The patient's medical history is unremarkable and she denied taking any drugs, vitamins, natural products, or blue-colored food stuff in the months before or during the event. The patient also denied contact with any product on skin, or wearing any clothes, blanket or tissue, whose blue color could be responsible for the finding. The clinical examination was normal. After asking the patient to exercise for 10 min on stairs, she presented with a vivid clear blue sweat covering her entire body (but not her face, palms, and soles) and staining her clothes (Figs 1–3). Even

after washing the blue sweat sites, it reappeared as blue color. The color was particularly noticeable in areas of close cutaneous tissue contact. The patient and her mother strongly denied any psychiatric disease, or any psychologically stressing situation, although they seemed very worried about the problem, with the patient's mother routinely canceling her outside appointments to stay at home with the daughter during the "crisis." Routine blood cells counts glycemia, liver function, seric iron, chrome and copper levels were within normal ranges.



Figure 1 Blue sweating after exercising



Figure 2 Paper blue sweating collected



Figure 3 Vivid blue color sweat

Skin biopsy showed no skin or sweat eccrine gland alterations. Urine samples were collected and analyzed with negative pigment findings. The patient was contacted for collection of sweat sample, but cancelled the appointment four times. On the last phone contact, 6 months after the first consultation, the patient reported that the blue sweat had disappeared, and there will be no more reasons to collect sweat samples.

### Discussion

Chromhidrosis is a very rare phenomenon with only a few cases described in the medical literature. According to Cilliers and de Beer, it can be divided into true eccrine chromhidrosis, apocrine chromhidrosis, and pseudo-eccrine chromhidrosis.<sup>3</sup>

True eccrine chromhidrosis occurs when water-soluble pigments, like dyes from the medicine quinine, are excreted via eccrine glands.<sup>4</sup>

Apocrine chromhidrosis is characterized by brown, black, green, or blue hidrosis, with axilla, facial, and areola targets sites.<sup>5,6</sup> Color chromhidrosis has been described in some ancient medicine texts. The first English case of chromhidrosis was published by Yonge of Plymouth in 1709. The author stated: "In this affection the colored sweating appears symmetrically in various parts of the body, the parts commonly affected being the cheeks, forehead, side of the nose, whole face, chest, abdomen, backs of the hands, finger-tips, and the flexors, flexures at the axillae, groins, and popliteal spaces. Although the color is generally black, nearly every color has been recorded."<sup>7</sup>

Shelley and Hurley<sup>8</sup> named oxidized lipofuscin as the intrinsic pigment possibly related to chromhidrosis. According to Cilliers and de Beer,<sup>3</sup> tyrosine, melanin, and heme breakdown products tend to be insoluble to fat solvents and can stain clothes from red to yellow, green, blue, and black. Shelley and Jurka in 1969 discussed the finding of purplish-blue sweating, in a 37-year-old woman, whose sweating stained her pillowcase during the night. The authors described the phenomenon as a localized chromhidrosis, which results from apocrine glands sweating, relating the affliction to an emotional stimulus. Juka states that true chromhidrosis is related to colored sweat (yellow, blue, brown, or black) caused by adrenergic apocrine stimulation.<sup>9</sup>

The patients discussed by these authors mainly have a localized type of chromhidrosis, typically corresponding to apocrine glands distribution. An extensive case of chromhidrosis was described in 1999 in South Africa. It was a 26-year-old patient with red chromhidrosis discovered to be caused by a tomato-flavored prepacked fast food.<sup>3</sup>

Pseudo-eccrine chromhidrosis occurs from surface compounds or molecules mixed with sweat, giving the seat a specific color. Pseudochromhidrosis can be accidental, as cited by Labouche, who described a group of students with localized foot black chromhidrosis, discovered to be associated

to a mix of sweat and pigments from particular school shoes, commonly used during the 1960s by students in France.<sup>10</sup>

Blue sweating has been reported among copper workers, whose sweat mixed with copper particles produced a blue-color sweat.<sup>3</sup> The analyzed patient, though, had no history of contact with copper or other heavy metals, and laboratory tests for heavy metals were negative.

A specific clinical picture of chromhidrosis happens when the patient applies substances to the skin in order to simulate a disease. It is referred to as dermatitis simulata, a subtype of dermatitis artefacta.<sup>11</sup> MacSween and Millard, in 2000, published a case of a young man who applied print ink to his skin, producing a green sweat, in order to simulate a disease. The authors advise attention to these patients' behavior, since psychiatric conditions could be associated with pseudo-eccrine chromhidrosis.<sup>12</sup> Pseudochromhidrosis can sometimes simulate apocrine chromhidrosis. In 2000, Thami and Kanwar described a 9-year-old girl with pseudochromhidrosis in her face simulating apocrine chromhidrosis.<sup>13</sup>

Pseudo-eccrine chromhidrosis was suspected for our patient as a possible diagnosis for months. Apocrine chromhidrosis was ruled out, because the chromhidrosis was intense, not localized, with an eccrine distribution pattern. The absence of alterations on clinical examination and laboratory tests and the vivid blue color of sweating ruled out the possibility of an internal chromhidrosis for the patient. The intermittent course of the affliction and the sparing of the face, hands, and feet also confirmed the diagnosis of pseudo-eccrine chromhidrosis. We could not rule out the possibility of an accidental pseudochromhidrosis, although the extent and intensity of the clinical picture drives this possibility to a lesser magnitude. As far as we know, this is the first case describing an extensive blue pigment as a cause of pseudo-eccrine chromhidrosis, even though the patient strongly denied the possible association of any product applied to the skin and the blue sweating. There were also no apparent characteristics of psychiatric disease, although the patient seemed happy with the fact that her mother, worried with the affliction, used to stay home with her during the "crisis." The avoidance of a sweat sample collection for spectrophotometric examination suggests the possibility of a hidden cause for the case, and leads us to inquire the possibility of a very rare kind of dermatitis simulata, a blue pseudo-eccrine chromhidrosis.

*Rubens Marcelo Souza Leite, MD*  
*Natalia Solon Nery, medical student*  
 Universidade Católica de Brasília, Brasília, Brazil

### References

- 1 Hurley HJ Jr. Apocrine chromhidrosis. In: Fitzpatrick TB, Eisen AZ, Wolff K, *et al.*, eds. *Dermatology in General Medicine*, 4th edn. New York: McGraw-Hill, 1993: 756.

- 2 Champion RH. Chromhidrosis. In: Champion RH, Burton JL, Burns DA, *et al.*, eds. *Textbook of Dermatology*, 6th edn. Oxford: Blackwell Science, 1998: 1985–2002.
- 3 Cilliers J, de Beer C. The case of the red lingerie – chromhidrosis revisited. *Dermatology* 1999; **199**: 149–152.
- 4 Hurley HJ, Wilkowsky J. Dye clearance and eccrine sweat secretion in human skin. *J Invest Dermatol* 1961; **36**: 259–272.
- 5 Dtaff DNM, Owens R, Kallin TA. Apocrine chromhidrosis involving the areola in a 15-year-old amateur skater. *Pediatr Dermatol* 1995; **12**: 48–50.
- 6 Schwartz T, Neumann R, Duschet P, *et al.* Apocrine chromhidrosis. *Hautarzt* 1989; **40**: 106–109.
- 7 Gould GM, Pyle WL. Physiologic and functional anomalies. In: *Anomalies and Curiosities of Medicine*. Philadelphia, 1896 (cited 2005 December 15). Available from: <<http://www.worldwideschool.org/library/books/tech/medicine/AnomaliesandCuriositiesofMedicine/chap9.html>>.
- 8 Sheley WB, Herley HJ. Localized chromhidrosis; a survey. *AMA Arch Dermatol Syphiligr* 1954; **69**: 449–471.
- 9 Shelley W, Jurka M. Mystery of the purple spotted pillowcase – chromhidrosis? *JAMA* 1969; **3**: 960.
- 10 Labouche F. Plantar pseudo chromhidrosis. *Bull Soc Fr Dermatol Syphiligr* 1965; **72**: 444–447.
- 11 King CM, Chalmers RJG. Another aspect of contrived disease: “dermatitis simulate.” *Cutis* 1984; **34**: 463–464.
- 12 MacSween RM, Millard LG. A green man. *Arch Dermatol* 2000; **136**: 115, 118.
- 13 Thami GP, Kanwar AJ. Red facial pseudochromhidrosis. *Br J Dermatol* 1982; **107**: 1219–1220.

#### Leg ulcers associated with factor V Leiden and prothrombin G20210A and methyltetrahydrofolate reductase mutations: successful treatment with warfarin

Chronic ulceration of the lower leg, including the foot, is a frequent condition, causing pain and social discomfort, and generating considerable costs.<sup>1</sup> The prevalence rate (all ulcers) ranges from 1% in the adult population to 5% in the population over 65 years of age.<sup>1</sup> The prevalence rate of venous leg ulcers in the > 65-year age group in the UK has been estimated to be 1–2%.<sup>2</sup> Thrombophilia is a risk factor for deep venous thrombosis, and deep venous thrombosis predisposes to chronic venous ulceration.<sup>3</sup> Patients with chronic venous ulceration have a prevalence rate of thrombophilia of 41%. This rate is 2–30-fold higher than the rate for the general population.<sup>4–6</sup>

We report a case of a 59-year-old white woman who presented for the evaluation and treatment of chronic leg ulceration. She reported the spontaneous development of three painful ulcers on the right leg (Fig. 1a) over the previous



**Figure 1** Ulcers before (a) and after (b) treatment with warfarin

5 months. She had been treated for two episodes of superficial thrombophlebitis in 2002 and 2006. No history of hypertension, diabetes, smoking, hormone therapy, previous surgery, immobilization, or previous deep venous thrombosis, and no family history of thrombosis, acute myocardial infarction, or stroke, were obtained. Cutaneous biopsy of the ulcer border showed venous stasis dermatitis. Bacterial, mycobacterial, and fungal cultures did not reveal any microorganisms. Doppler ultrasound showed no evidence of deep venous insufficiency. Thrombophilia screening disclosed factor V Leiden, prothrombin gene mutation (G20210A), and methyltetrahydrofolate reductase (MTHFR) mutation, all in the heterozygote form, and a high level of anticardiolipin antibody class immunoglobulin M (IgM) [40 IgM phospholipid units (MPL); normal value, < 20 MPL]. She presented normal levels of antithrombin III, cryoglobulins, cryoagglutinins, apolipoprotein A1, proteins C and S, fibrinogen, homocysteine, and lupus anticoagulant. Three days after having started warfarin therapy, 5 mg orally daily, the pain symptoms improved, and the cutaneous ulcers resolved with scars 2 weeks later (Fig. 1b). The international normalized ratio (INR) was maintained between 2.5 and 3.0.

Hypercoagulable disorders may cause ulceration, either indirectly as a consequence of venous thrombosis, or directly by thrombus formation in small arteries, arterioles, capillaries, or venules.<sup>1</sup> A growing number of hereditary or acquired conditions predisposing to thrombosis have been identified, such as the antiphospholipid syndrome, deficiency of antithrombin III, deficiency of protein C or protein S, or abnormal clotting factors (factor V Leiden, prothrombin gene mutation).<sup>1</sup> It is not the laboratory abnormalities, but the specific clinical picture that determines whether a patient should be treated with anticoagulant drugs.<sup>1</sup> In Brazil, the prevalence of factor V Leiden is 2% of the population, and 6–20% of the population suffer from venous thromboembolism in our environment.<sup>7</sup> In France, Ribeau *et al.*<sup>8</sup> studied 35 patients with venous leg ulcers, and concluded that the prevalence of coagulation