Blue Pseudochromhidrosis Secondary to Topiramate Treatment

Emeline Castela[1], Pierre Thomas[2], Valérie Bronsard[1], Jean-Philippe Lacour[1], Jean-Paul Ortonne[1] and Thierry Passeron[1]
Departments of [1]Dermatology and [2]Neurology, University Hospital of Nice, Hôpital Archet 2, Rte de St-Antoine de Ginestière, FR-06200 Nice, France.
E-mail: passeron@unice.fr
Accepted May 18, 2009.

Sir,

Topiramate (TPR) is an adjunctive treatment for patients with refractory epilepsy. Several cases of hypohidrosis under TPR treatment have been reported. We describe here a new reversible side-effect on human sweating function: blue pseudochromhidrosis. Chromhidrosis and pseudochromhidrosis are rare skin disorders. Chromhidrosis refers to the excretion by the apocrine glands of sweat containing lipofuscin pigments, while the terms of pseudochromhidrosis or extrinsic chromhidrosis are used when the eccrine sweat is coloured on the surface of the skin as a result of the deposit of extrinsic dyes or paints, or by the transformation by chromogenic bacteria.

CASE REPORT

A 28-year-old woman presented with a sudden blue discoloration of the skin. She had had epilepsy since the age of 18 years, and syndromic diagnosis was consistent with epilepsy with tonic-clonic seizures only. She was initially treated with valproate, 1500 mg a day, but weight gain led to poor compliance that led to alternative monotherapy with levetinacetam, 1 g/day. Persistence of seizures led to combination therapy with TPR, 150 mg/day, which was increased to 200 mg/day 4 months previously. She reported no change in her habits or way of dressing, but reported that she had got drunk the day before the eruption. On examination, there was an odourless blue discoloration of the skin, which become yellowish under the Wood's lamp. The discoloration was located on the arms, forearms, elbows, and was extending to the face and the thorax (Figs 1 and 2). The coloration rubbed out with a damp cotton swab. Urine, saliva and tear colour was normal. The sweat pH on the surface, measured with a pH meter, was slightly decreased: on the arms and the elbows (5.1), and 6 on the rest of the body (normal range 5.2–7). Blood test found a hyperchloraemia (111 mmol/l) and a decrease in bicarbonate levels (18 mmol/l). Skin scrapings found positive *Bacillus* species, and the search for *Malassezia furfur* was negative. We diagnosed a pseudochromhidrosis. An incomplete improvement in symptoms was obtained with symptomatic treatment (basic soap and topical erythromycin). Abnormal skin colouration resolved a few weeks later when TPR treatment was spontaneously discontinued by the patient and new flares were observed when it was reintroduced.

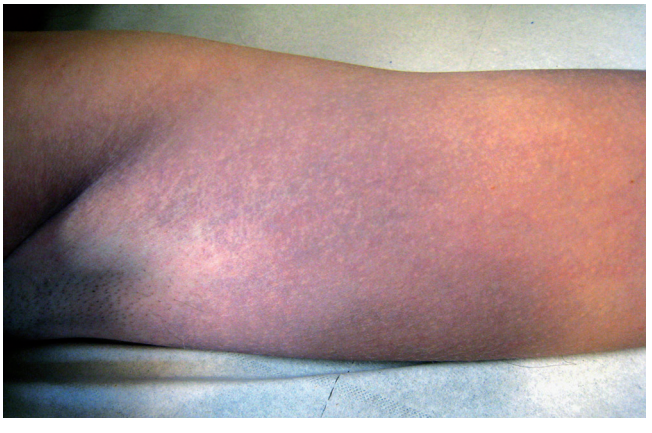

Fig. 1. Blue discoloration of the arm.

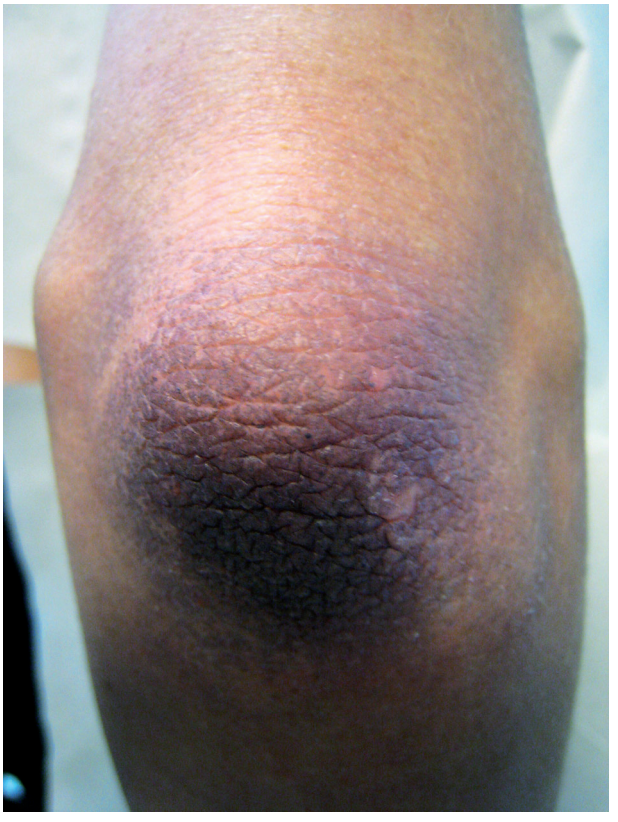

Fig. 2. Reinforcement of the blue discoloration on the elbow.

DISCUSSION

TPR is an inhibitor of the carbonic anhydrase (CA) isoenzymes II and IV that is currently used to treat epilepsy (1, 2). Those enzymes are also expressed in the kidney and in the sudoral eccrine glands. Tubular acidosis has

 doi: 10.2340/00015555-0696
Journal Compilation © 2009 Acta Dermato-Venereologica. ISSN 0001-5555

been reported after TPR treatment (3). On the other hand, hypohidrosis is a dose-dependent, reversible side-effect of TPR that usually occurs about 5 months after the introduction of the drug (4, 5). In most cases, hypohidrosis is not symptomatic, but it sometimes leads to heat intolerance and hyperthermia. This side-effect was first described in children, but can also occur in adults. The mechanism underlying this effect is unclear. An inhibition of CA was initially suspected. This enzyme is implicated in the acid-base balance and its inhibition might alter the primary sweat composition and reduce the water formation. Recent data suggests that the decreased sweat secretion induced by TPR could be due to a reduced aquaporin-5 (AQP5) expression. AQP5 is a member of the aquaporin family of water-selective pores, which is present in sweat glands. Indeed, mice, which received TPR during 4 weeks do not differ from controls in average secretory coil diameter, CA II expression and CA activity. In contrast, anhidrotic mice do show a reduction in membrane AQP5 expression in sweat glands after TPR delivery (6). In our patient, TPR imputability in the occurrence of this pseudochromhidrosis is supported by the introduction delay (4 months after increasing the doses), which is similar to those reported for hypohidrosis, and the absence of any other precipitating factors. Finally, the regression of the symptoms after treatment was stopped and the new flares after its reintroduction strongly support the responsibility of TPR. Hyperchloraemia, which reflects the carbonic anhydrase inhibition and traduces a compensated metabolic acidosis, as well as the moderate decrease in the sweat pH, also plead for its responsibility.

Only a few fungi and bacteria are known to induce pseudochromhidrosis. Corynebacteria are responsible for red pseudochromhidrosis, whereas *M. furfur* and *Bacillus spp.* are the agents involved in the blue pseudochromhidrosis. The ecological stability of these commensal bacteria in different body sites rely on environmental factors, such as hydration, oxygen, growth substrates and the pH of the stratum corneum. Hypohidrosis and sweat pH modification can trigger the proliferation of chromogene bacteria on the skin, such as *M. furfur* and *Bacillus spp*. Deregulation of the skin pH due to systemic treatments was only reported once to induce a pseudochromhidrosis: in a single case report the association of lansoprazole, a proton pump inhibitor, and ranitidine, a type two histamine receptor antagonist, triggered the proliferation of *M. furfur* and *Bacillus spp.* and led to a blue pseudochromhidrosis (7).

Pseudochromhidrosis is a rare reversible side-effect of TPR, related to its action on sweat glands. Although benign, it can significantly alter the quality of life and may cause social impairment. Physicians should be aware of this potential side-effect.

The authors declare no conflict of interest.

REFERENCES

1. Shank RP, Smith-Swintosky VL, Maryanoff BE. Carbonic anhydrase inhibition. Insight into the characteristics of zonisamide, topiramate, and the sulfamide cognate of topiramate. J Enzym Inhib Med Chem 2008; 23: 271–276.
2. Dodgson SJ, Shank RP, Maryanoff BE. Topiramate as an inhibitor of carbonic anhydrase isoenzymes. Epilepsia 2000; 41 Suppl 1: S35–S39.
3. Mathews KD, Stark JE. Hyperchloremic, normal anion-gap, metabolic acidosis due to topiramate. Am J Health Syst Pharm 2008; 65: 1430–1434.
4. Arcas J, Ferrer T, Roche MC, Martinez-Bermejo A, Lopez-Martin V. Hypohidrosis related to the administration of topiramate to children. Epilepsia 2001; 42: 1363–1365.
5. de Carolis P, Magnifico F, Pierangeli G, Rinaldi R, Galeotti M, Cevoli S, et al. Transient hypohidrosis induced by topiramate. Epilepsia 2003; 44: 974–976.
6. Ma L, Huang YG, Deng YC, Tian JY, Rao ZR, Che HL, et al. Topiramate reduced sweat secretion and aquaporin-5 expression in sweat glands of mice. Life Sci 2007; 80: 2461–2468.
7. Hill S, Duffill M, Lamont D, Rademaker M, Yung A. Pseudochromhidrosis: blue discolouration of the head and neck. Australas J Dermatol 2007; 48: 239–241.